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THE ELECTRICAL REACTIONS OF MUSCLES BEFORE AND AFTER NERVE INJURY.

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WHEN the nerve leading to a muscle is damaged or destroyed, the muscle shows in its response to the electric current a series of changes which are grouped together under the name "reaction of degeneration." These changes may be classed conveniently under two heads: (1) changes in the character of the electric current required to excite the muscle; and (2) changes in the response of the muscle to excitation. The changes in the response consist in the reduced rapidity, slow subsidence and weak power of the contraction, and sometimes in its localization to the neighbourhood of the electrodes. These suffice to give a rough idea of the state of the muscle, but it is very doubtful if the most exact measurements of them would give information which could be regarded as quantitative, since they depend not only on the degree of degeneration, but also on such transitory conditions as the temperature of the limb, whether it has been massaged recently or not, &c.

In regard to the changes classed under the first head, the position seems more hopeful, and in recent years more and more stress has been laid on the measurement of the current required to excite, as giving a true indication of the state of the muscle and its nerve. It is the purpose of the present inquiry to find out if possible more exactly the relation between the state of the muscle and the nature of the current required to excite it, to investigate the causes underlying this relation, and to see how much diagnostic information may be gained by the different methods at present in vogue.

In the ordinary method of testing with faradic and galvanic currents,

the stimulus may be varied at will as regards its strength but not as regards its duration. The faradic current rises rapidly to its maximum in about 0.0001 second (the exact constants depending on the dimensions of the coil) and falls more slowly to zero. In practice the current is repeated many times a second, but this is simply a matter of convenience, as it allows the contraction to be more easily observed—the muscle responds as readily to a single shock as it does to a series of shocks. The galvanic current rises instantaneously to its maximum value and remains at the same level until it is turned off. Without special apparatus its duration cannot be controlled if it is much less than $\frac{1}{2}$ second, and if it is greater than this its duration makes no difference to the efficacy of the current. Thus we are confined to a very brief current and a very long one, and there is nothing between the two. With this arrangement it is easy to tell whether the nerve to a muscle is damaged or not, since a muscle with intact nerve supply will respond to the brief faradic current, whereas one with a damaged nerve supply will not respond to this, but will respond to the longer galvanic current. However, this information is entirely qualitative, and it does not allow us to make any estimate of the exact state of affairs. Some additional information may be gained from the alterations in the strength of the current required to excite, but unfortunately such changes may be due to altered skin resistance, increase of fluid in the subcutaneous tissues, &c., quite apart from any change in the condition of the nerve supply. At the same time, it is clear that the degeneration of the nerve causes an increase in the duration of the current required to excite the muscle, and this suggests that if we could measure the least effective duration it might give valuable quantitative information about the condition of the muscle and nerve.

For this purpose the method of condenser discharges has been introduced by Cluzet [1] in France and Lewis Jones [3] in this country. This method depends on the fact that the discharge of a condenser through a constant resistance varies in duration according to the capacity of the condenser. The discharge starts at its maximum value and falls off gradually, and with the sets of condensers in use at present it is possible to obtain currents whose total duration varies from 0.00004 second to 0.005 second. By inserting special resistances even longer discharges may be obtained. With these currents it is found that the more severe the injury to the nerve appears to be, the greater is the capacity of the condenser (and therefore the longer is the duration

of the discharge) required to excite the muscle. Thus the method would seem to give all the information which could be desired from a clinical point of view: we have only to find the least capacity of condenser which will excite the muscle, and this will give a measure of the severity of the injury. Unfortunately, the principles which underlie this method have never been thoroughly decided, and the conclusions which are based on it are derived almost entirely from observations on the human being, and very little from experimental work on animals or on isolated muscle and nerve preparations. Indeed, two years ago Laugier [5] pointed out that a consideration of the facts which are known in regard to the electrical stimulation of cold-blooded tissues shows that there is a serious fallacy in the condenser method as it is used at present. These facts are stated briefly in the following section.

THE RELATION OF CURRENT STRENGTH TO CURRENT DURATION IN COLD-BLOODED TISSUES.

Within the last ten years the precise conditions under which an electrical current will stimulate the excitable tissues of cold-blooded animals have been worked out with some approach to certainty. The relations between the condition of the tissue, the form of the current, its strength and its duration have been studied exhaustively and reduced to mathematical terms by Keith Lucas [7], Lapicque [4], A. V. Hill [2], and others, and though there is still some difference of opinion as to the theoretical interpretation of these relations, their exact form is no longer in doubt. The most fruitful results have been obtained by the use of constant currents, that is, of currents whose strength rises immediately to a fixed value and remains at that value as long as the current is flowing. In such currents there are only two variables to consider, the strength and the duration, and both of these are easily controlled. When these currents are applied to a simple tissue, such as the sciatic nerve of the frog, it is found that currents of less than a certain minimal duration will not excite, however strong they may be; with longer currents the strength required to excite becomes less and less as the duration increases, until eventually it falls to a constant level which cannot be reduced further by increasing the duration. This relation is shown in fig. 1, which is constructed from an experiment by Keith Lucas [6] on the sartorius muscle of the toad. In this case, however strong the current may be it will not excite at all if its duration is less than 0.003 second. With slightly longer durations a

very strong current is needed, and the strength falls off gradually as the duration is increased. Eventually the minimal strength is reached, and when the potential difference is less than 0.076 volt the current will not excite, however long its duration may be. Thus the current which will excite the muscle must possess a duration longer than 0.003 second and a strength greater than that given by 0.076 volt. In between these limiting values the relation between strength and duration is expressed by a curve which is convex to the origin.

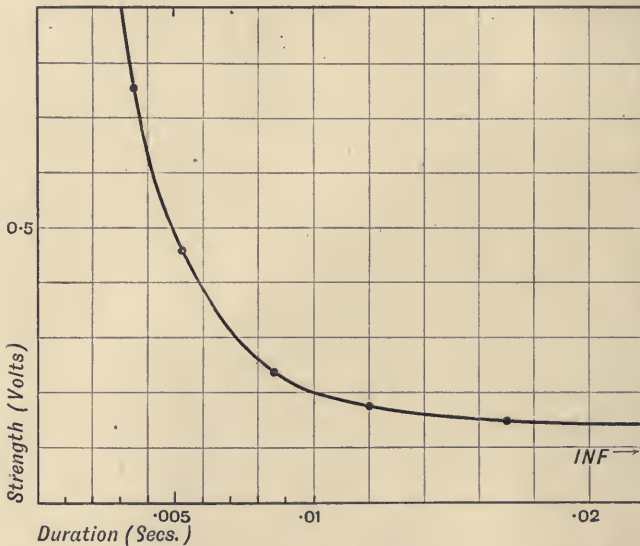


FIG. 1. Relation between strength and duration of current required to excite the sartorius muscle of the toad. (Keith Lucas.)

A curve which is almost identical with fig. 1 is found for every preparation of the toad's sartorius, the only difference being that the minimal current strength required to excite will naturally depend on the resistance of the muscle, the dimensions of the electrodes, &c. In every case the current required to excite begins to increase when the duration is reduced much below 0.02 second, and is doubled when the duration is about 0.01 second. This holds good for the sartorius of the frog as well as that of the toad, and for the gastrocnemius as well as the sartorius. A curve of the same form is given by the sciatic nerve of the frog or toad and by the nerve-fibres in the substance of the muscles, but in this case the time-factor is much less important and the minimal strength does not begin to rise until the duration is less

than about 0.003 second. Ventricular muscle shows a much slower reaction than voluntary muscle, the minimal strength rising at about 2.0 seconds. In every case which has been examined (and this includes the muscles and nerves of a variety of cold-blooded animals) the curve is of the same form, and is approximately constant for similar tissues under similar conditions.

Various equations have been found to fit the curve. That of Weiss [12] is the simplest and that of A. V. Hill [2] conforms most accurately to the experimental results. Weiss's equation is:—

$$i = a + bt,$$

where i is the current strength, t the duration, and a and b are constants. Hill's equation is:—

$$i = \frac{\lambda}{1 - \mu\theta^t}$$

where λ , μ and θ are constants. The constants are easily calculated in either case, and in Hill's equation they are given a definite physical interpretation. However, for all practical purposes the curve may be defined by two factors, one of which is the least current required to excite at infinite duration, and the other a time-factor depending on the "rapidity" of the tissue. This factor is given approximately by the duration at which the current strength must be doubled, a quantity which is equal to the ratio $\frac{a}{b}$ in Weiss's equation. Lapicque has proposed the name "chronaxie" for this quantity, and his nomenclature will be adopted in the following discussion. It follows, then, that for any given tissue a determination of the duration at which the current strength must be doubled suffices to fix the strength-duration curve for that tissue.

The characteristics of this curve have been insisted on at some length because of its great importance in connexion with electro-diagnosis. In the first place, it is clear that the least duration which a current must possess if it is to stimulate the excitable tissues of a cold-blooded animal depends not only on the nature and condition of the tissue, but also on the strength of the current. A strong current will excite at very much shorter durations than a weak current. The same holds good for condenser discharges as for constant currents, and therefore the least effective duration of a condenser discharge will depend on the strength of the discharge as well as on the state of the tissue to which it is applied, and if the excitability of the tissue happens to change, the least effective duration corresponding to a given

strength of current will change too. If the same reasoning can be applied to mammalian muscles and nerves, it is clear that the method of condenser discharges cannot give a true indication of the state of affairs unless precautions are taken that the strength of the discharge shall always bear the same relation to the strength required when the duration is infinitely long. In the ordinary condenser method this precaution is not taken, and Laugier's criticism of the method rests on this ground. Clearly, then, to make sure that this objection is valid it is important to find out how far the relation expressed in Weiss's or Hill's equation is true for mammalian as well as for cold-blooded tissues.

The determination of the strength-duration curve is important for another reason. In the cold-blooded tissues the time factor of the curve, the "chronaxie," is constant for similar tissues examined under similar conditions, and differs greatly from one tissue to another. Thus the determination of the curve makes it possible to distinguish clearly the nature of the tissue upon which the stimulus takes effect. For instance, it is possible to tell whether the current applied to a muscle stimulates the muscle-fibres directly or indirectly through the medium of the intramuscular nerve-fibres. The value of this will be seen hereafter.

THE RELATION BETWEEN CURRENT STRENGTH AND CURRENT DURATION IN HEALTHY MUSCLES.

The apparatus required for the determination of the strength-duration curve in human subjects must be capable of delivering a constant current varying in duration from $\frac{1}{10000}$ second to $\frac{1}{10}$ second and at a potential varying from 1 to 100 volts or more. In practice the duration was controlled by a Lucas pendulum [10], and the potential by a potentiometer connected to the 200-volt mains (continuous). The potentiometer consisted of two dial resistance boxes, the resistance in the two together being maintained at a constant value of 1,000 ohms. The current was led off from the potentiometer through a 500-ohm resistance to the stimulating electrodes. This resistance was inserted to cut down the current which would otherwise pass when the short-circuit key, K_1 , is closed. In the circuit from the potentiometer were two knock-down keys, one in the circuit through the patient and the other in a short circuit which avoided the patient and returned the current direct to the potentiometer. The two keys were opened by means of the pendulum, and the interval separating their opening could be varied from 0.0001 second to 0.2 second. The arrange-

ment of the connexions is shown in fig. 2. The resistance boxes are lettered A, B, and C, and the keys K_1 and K_2 . When the short-circuit key, K_1 , is opened by the pendulum, the current begins to flow through the patient, and when the in-circuit key K_2 , is opened, the flow ceases. By altering the ratio of the resistances in the two halves of the potentiometer, the potential difference between the points A and B can be varied from 1 to 200 volts. Thus both current strength and current duration can be varied within fairly wide limits. The whole arrangement is practically identical with that devised by Keith Lucas [9] for use in his experiments on cold-blooded tissues. No attempt was made to measure the current directly; this is not essential, since all we require to know is the strength compared with that required to excite when the duration is infinitely long; furthermore, it is impossible to measure the strength without using a ballistic galvanometer or some such method, since the currents are too short in duration to affect the usual measuring instruments, and too strong to be borne comfortably by the patient if they are allowed to run for any length of time.

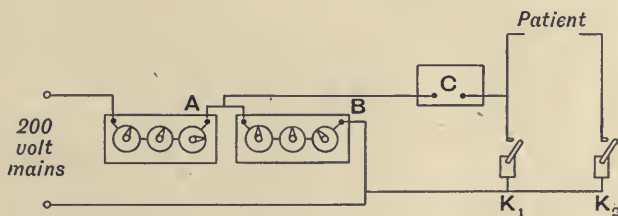


FIG. 2.--Apparatus for delivering constant currents of variable strength and duration.

In the following experiments the current strength is always expressed as a multiple of that required to excite when the duration lasts for several seconds. This is given the value 10, and is spoken of as the strength at infinite duration, for when the duration exceeds one or two seconds its exact value is found to make no difference to the strength.

The majority of experiments to be described were made on the tibialis anticus muscle. This is an ideal muscle for the purpose as it is easily excited and its contractions are easily observed and distinguished from those of neighbouring muscles. Moreover, it is frequently paralysed in injuries of the sciatic, poliomyelitis, &c. In working with this muscle a large pad electrode was placed under the calf to serve as the anode, and a small pad, 1 in. square, was bandaged on to the front of the leg for the kathode. The exact position of this was found to be

unimportant, but as a rule it was secured with its centre 1 in. from the anterior border of the tibia and 2 in. below the level of the head of the fibula. Both electrodes were soaked in a solution of ammonium chloride. With this arrangement the strength of current required to excite at infinite duration does not vary by more than 5 per cent. during a series of measurements lasting twenty minutes or more. The contraction of the muscle is best detected by placing the index-finger across the surface of the muscle with its tip resting on the border of the tibia. The contraction of those fibres lying immediately external to the tibia can be felt by this method when their contraction is too weak to produce any movement of the foot or any visible deformation of the skin.

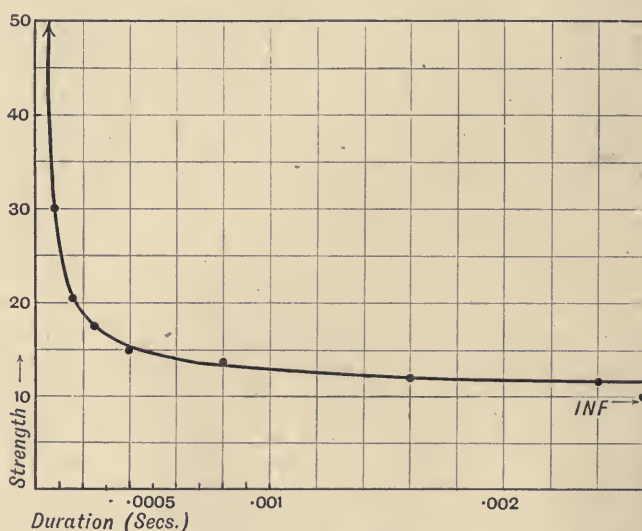


FIG. 3.—Strength-duration curve for human tibialis anticus with intact nerve supply.

The strength-duration curves were always determined in the following way: First of all the current was made and broken after an interval of some seconds by a hand switch, and the potentiometer was adjusted so that the current was just strong enough to produce a contraction. This gave the strength at infinite duration. If this appeared to be constant after several measurements, the pendulum was set to give a current lasting for about 0.1 second, and the requisite strength was redetermined. The duration was reduced still further and the strength required to excite was determined for each duration, until eventually the duration was so short that currents five or six times the value at infinite duration failed to excite the muscle. The duration was then

increased to check the previous results, and, finally, the strength at infinite duration was determined again. As a rule, the results of the two sets of readings with the duration decreasing and increasing agree very well, the difference in two readings at the same duration being rarely greater than 5 per cent., and usually less.

A typical curve for the tibialis anticus with intact nerve supply is shown in fig. 3. In this and in all subsequent figures the current strength is shown by the ordinates, the strength at infinite duration being given the value 10, and other strengths expressed as multiples of this. The duration of the current is shown by the abscissæ. In the present case it will be seen that the curve rises very gradually until the duration is reduced to about 0·0003 second. As the duration is reduced still further, the curve rises very rapidly, and at 0·0001 second a current over three times as strong as that at infinite duration is required to produce a contraction. As the significant durations are so short and the probable error is large, it is difficult to be certain as to the precise form of the curve, but the current strength appears to be doubled at a duration of about 0·00018 second. Thus the chronaxie in this case is 0·00018 second. A value which varies between 0·00025 second and 0·00008 second was found in all the healthy muscles examined, and this holds good not only for the tibialis anticus, but for all the other muscles which were investigated—the biceps, the flexors and extensors of the forearm, the extensors of the thigh and the small muscles of the thumb.

The actual values of the chronaxie for healthy muscles in six different individuals are shown in Table I. When the kathode is applied to a nerve-trunk instead of to a muscle, the chronaxie is on the whole slightly longer. In the case of the external popliteal nerve the average of four determinations gave 0·00025 second. However, the measurement is more difficult than in the case of a muscle, and for this reason the difference cannot be insisted upon.

TABLE I.—CHRONAXIE OF MUSCLES WITH INTACT NERVE SUPPLY.

Muscle	Subject	Chronaxie
Tibialis anticus	a ..	0·00016 second.
"	b ..	0·00008 "
"	c ..	0·00015 "
"	d ..	0·00025 "
"	e ..	0·00016 "
Biceps	a ..	0·00012 "
"	b ..	0·00020 "
Extensor longus digitorum..	b ..	0·00024 "
"	e ..	0·00010 "
Tensor fasciæ femoris ..	a ..	0·00008 "
"	b ..	0·00015 "
Average value for all muscles	0·00016 "

THE STRENGTH-DURATION CURVE IN DENERVATED MUSCLES.

The simplest case to consider is one in which there has been a complete section of the nerve, the muscle being examined at a time when all the nerve-fibres peripheral to the injury must have degenerated and before there are any signs of recovery. The observations to be recorded in the present section were made on the tibialis anticus at different times after the section of the sciatic or external popliteal nerve. Records were made from four patients showing the syndrome of complete sciatic division (due to gunshot wounds), and in three of these the division of the nerve was verified by operation. The fifth case is one of injury to the external popliteal. The following is a short summary of the cases :—

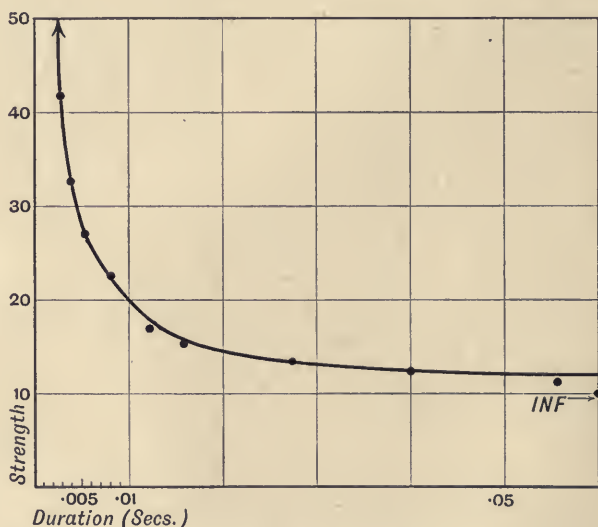


FIG. 4.—Tibialis anticus six months after division of sciatic.

Case 1.—The patient was shot through the right leg on March 10, 1915. There was complete paralysis of all the muscles below the knee and complete sensory loss over the area supplied by the sciatic. There was no pain and not much wasting of the muscles. Tested in the ordinary way, the tibialis anticus showed the complete reaction of degeneration. As there were no signs of recovery, the sciatic was exposed on October 30, 1915, and it was found to be completely divided, with a gap of $2\frac{1}{2}$ in. between the ends. Fig. 4 shows the strength-duration curve determined on September 28. The curve is of the same form as that in figs. 1 and 3, but the slope is much more gradual, and the current strength is doubled at 0.0095 second and increased to five times the threshold

value at 0.0027 second. Thus the chronaxie is 0.0095 second. In the other leg, which was uninjured, the tibialis anticus gave a chronaxie of 0.00012 second, the usual value for muscle with intact nerve supply. Thus the chronaxie of the denervated muscle is nearly 100 times as long as that of the corresponding healthy muscle. The determination was repeated on December 4, nearly two months after the operation and three months after the first determination. The curve coincides within the limits of error with the earlier determination, the chronaxie being 0.011 second.

Case 2.—In this patient the left sciatic was wounded in March, 1915, and a month later the wound was opened and a portion of the nerve which had been converted into scar tissue was removed and the ends of the nerve were sutured. There was the usual motor and sensory loss, and there were no signs of recovery when he was examined. The curve was determined on September 17, 1915, and again on September 30. In both cases the chronaxie was 0.011 second and the curves were almost identical with those in Case 1.

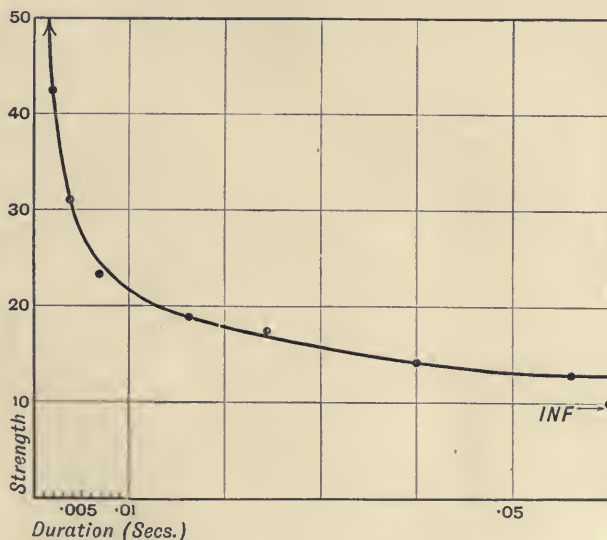


FIG. 5.—Tibialis anticus one and a half months after division of sciatic.

Case 3.—The leg was shot through in September, 1915, and the sciatic was exposed on October 11 and found to be divided. The ends were cleaned and sutured, and the curve was determined on November 3 and again on December 10. The chronaxie had the value 0.013 second at the first determination and 0.010 second at the second. For very strong currents the limiting durations are shorter than in Case 1, but otherwise the agreement is very close. The curve for November 3 is shown in fig. 5.

Case 4.—The patient was shot through the lumbo-sacral plexus on the right side in May, 1915, and had all the signs of complete division of the sciatic.

He was examined once at the beginning of September and again a month later. The chronaxie was 0.010 second at the first determination and 0.0095 second at the second. There were no signs of recovery when the patient was discharged, but the condition of the nerve was never verified by operation.

Case 5.—The patient's fibula was fractured at its head by a bullet in June, 1915, and there was at once complete paralysis of the muscles supplied by the external popliteal. There was no recovery when he was examined on November 4. The chronaxie in this case was 0.013 second, and the curve agrees closely with those in figs. 4 and 5.

The different values of the chronaxie in these cases are collected in Table II, and it will be seen that they give a mean value of 0.011 second with extremes of 0.013 second and 0.0095 second.

From one point of view these results are only what might have been expected. The muscles had lost their response to faradic currents and retained that to galvanic currents, and therefore it is not surprising that the least duration of current which is necessary to excite them is very much longer than it is in a muscle with intact nerve supply. The form of the curve remains essentially the same though the time constant is altered, and this again is not to be wondered at in view of the fact that the same form of curve has been found for every excitable tissue which has been investigated hitherto.

From another point of view the results are certainly unexpected. In all, nine curves were determined in five different subjects at intervals varying from six weeks to nine months after the division of the nerve. In all these determinations the chronaxie was never greater than 0.013 second and never less than 0.0095 second. It is true that in every case the leg had been treated with daily massage, passive movements and galvanism very soon after the injury had occurred; but even so, it is surprising to find that the nature of the current required to excite varies so little with the lapse of time. As a matter of fact, the temporary condition of the muscle at the moment when it is examined does not affect the curve in the least. This is shown by some observations which were made on Case 1 to test the immediate effect of massage and exercise. The right tibialis anticus was examined at 9.30 a.m. before the leg was massaged, and the chronaxie was found to be 0.011 second. The leg was left motionless and exposed to cold air until 11.15 a.m. The curve was redetermined and was found to coincide with the first measurement. The leg was then massaged and exercised thoroughly for half an hour, and at 12.20 p.m. the curve was determined again. The chronaxie was still 0.011 second and the curve

had not altered in the least, although the contraction was certainly less sluggish than it had been before the massage. Clearly, then, the curve is not affected by such transitory conditions as the temperature and state of activity of the muscle at the moment when the determination is made, and some other cause must be looked for to explain the constancy of the results with different muscles. Either we must suppose that the excitability constants do not vary as the condition of the muscle passes from bad to worse, or else the condition of the muscle does not change appreciably within the time limits investigated.

The question is cleared up to some extent by the results given by muscles to which voluntary power is returning after an incomplete injury to the nerve. These are discussed in the following section.

TABLE II.—TIBIALIS ANTICUS AFTER COMPLETE DIVISION OF THE SCIATIC WITH NO SIGNS OF RECOVERY.

Case		Time after injury				Chronaxie
1	..	a, 6 months	0·0095 second.
		b, 9 "	0·011 "
2	..	a, 6 "	0·011 "
		b, 6½ "	0·011 "
3	..	a, 1½ "	0·013 "
		b, 2½ "	0·010 "
4	..	a, 4 "	0·010 "
		b, 5 "	0·0095 "
5	..	a, 5 "	(external popliteal)	0·013 "
			Mean value	0·011 "

In Cases 1, 2 and 3 the section of the nerve was verified by operation.

THE STRENGTH-DURATION CURVE IN CASES SHOWING EVIDENCE OF RECOVERY.

The foregoing results show that in the healthy tibialis anticus with intact nerve supply the strength of current required to excite is doubled when the duration is reduced to 0·0003 second — 0·00008 second, whereas, if the nerve has degenerated, the duration at which the strength is doubled is about 0·011 second. Both cases give a curve of the same type, but the curve falls much more slowly in the latter case than in the former. To understand the significance of these curves it is clearly important to find out what happens when recovery is taking place, how the slow curve for denervated muscle becomes transformed into the rapid curve characteristic of muscle with intact nerve supply.

The ideal case to investigate would be one in which there had been a complete section of the nerve, with subsequent regeneration and commencing return of voluntary power. However, the sciatic takes many months to regenerate, and patients with complete sciatic division

are usually discharged long before there are any signs of recovery. The ulnar and median divided near the wrist recover much more rapidly, but the small muscles of the hand are very difficult to investigate by the present method on account of the spread of the current to neighbouring healthy muscles. Consequently the cases in the present section are limited to two of acute anterior poliomyelitis, one of toxic polyneuritis of unknown origin and one of incomplete injury to the sciatic by bullet wound. In all these cases the tibialis anticus had been completely paralysed, and at the time of investigation voluntary power had just returned in some degree to it or to neighbouring muscles.

The following is a short abstract of these cases :—

Case 6.—The patient, aged 19, had a typical attack of acute anterior poliomyelitis, beginning on September 5, 1915. When he was first examined there was moderate power in the arms, but very little in the trunk or legs. Power in the legs returned gradually during the months of November and December when he was under observation. The muscles were examined electrically on November 27, December 8, and December 26. During the whole of this time there was no response to faradism in the right tibialis anticus, and in the left there was a slight response to very strong currents. A slight degree of voluntary power was present on either side, but the left tibialis anticus was always stronger than the right and its power improved more rapidly. The determinations on November 27 and December 8 are shown in figs. 6 and 7. The curve for the right tibialis anticus is drawn as an unbroken line and that for the left is interrupted. All these curves show an obvious discontinuity and are composed of two simple curves of the same form but different constants. In fig. 6, for instance, in the curve for the right tibialis anticus there is a discontinuity when the duration is reduced to 0.0008 second and the strength has risen to 62. At this point the curve suddenly becomes horizontal and the strength remains constant at 62 until the duration has fallen to 0.0002 second. A further slight decrease in duration causes a sudden rise in the strength. In the curve for the left tibialis anticus the discontinuity occurs when the duration is 0.0024 second and the strength 35, and the curve does not begin to rise steeply again until the duration has fallen to 0.00024 second. In fig. 7 the discontinuities occur at longer durations and smaller current strengths. That for the right leg begins at a duration of 0.0017 second and a strength of 40, and that for the left at a duration of 0.0032 second and a strength of 29. The curves had not changed appreciably from this at the third determination on December 26.

Case 7.—This is the case of a patient, aged 28, who had an attack of acute poliomyelitis on October 8, 1915. The paralysis remained in the trunk, right arm and legs. He was examined on December 27, 1915. At this date the left tibialis anticus had moderate voluntary power, but did not react to faradism applied in the region of the motor point unless a very strong current was used.

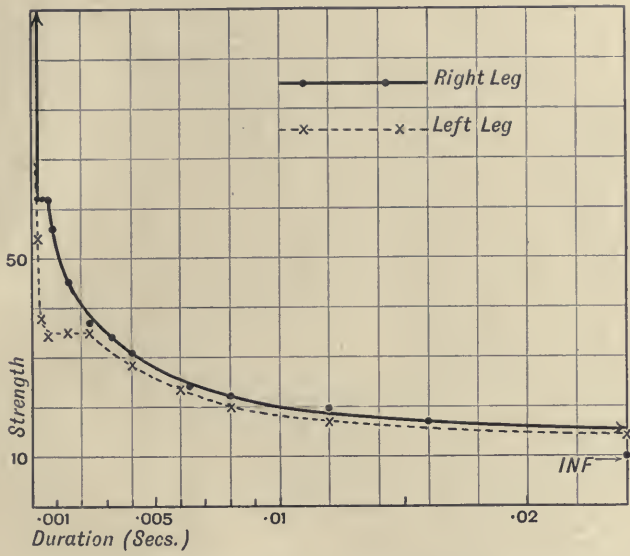


FIG. 6.—Tibialis anticus recovering from poliomyelitis.

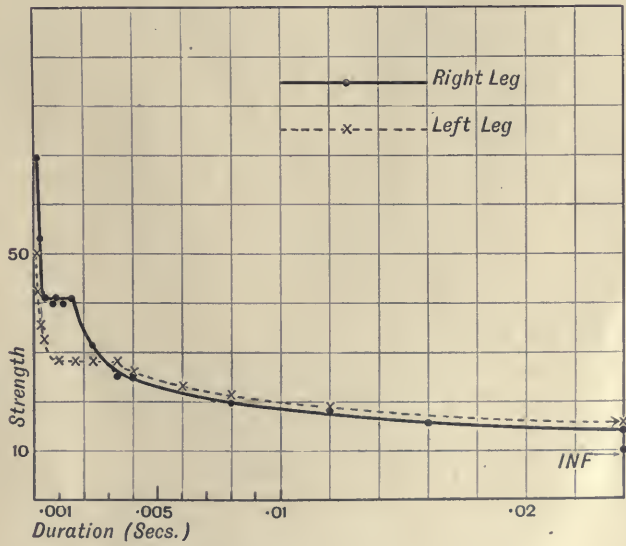


FIG. 7.—Same case as fig. 6, eleven days later.

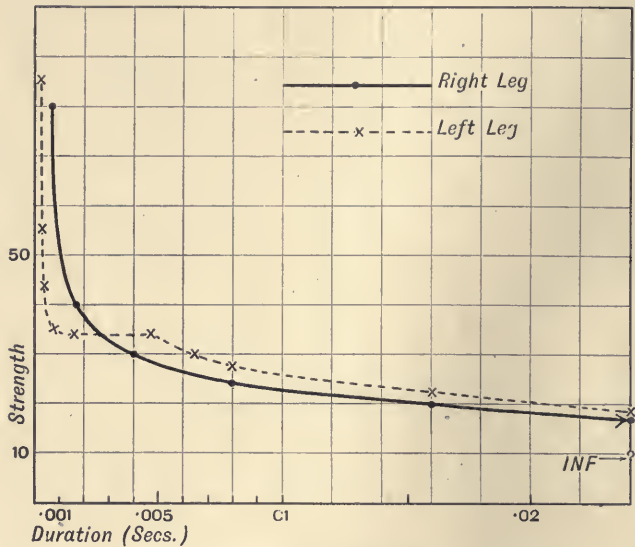


FIG. 8.—Poliomyelitis : slight return of power in left tibialis anticus, none in right.

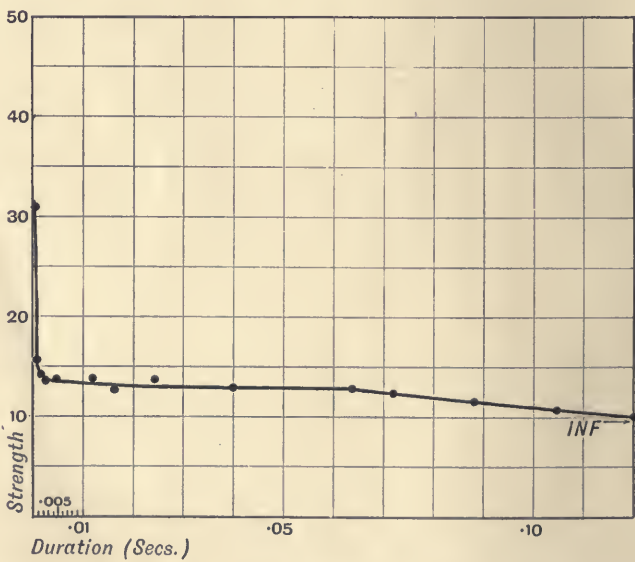


FIG. 9.—Same case as fig. 8 : left tibialis anticus stimulated nearer the tendon.

It reacted more readily when the current was applied lower down the leg. The right tibialis anticus had no voluntary power at all and did not react to the strongest faradic currents which could be used. Fig. 8 shows the curves for both legs with the kathode applied high up near the motor point. That for the left tibialis anticus is drawn as an interrupted, and that for the right as an unbroken line. The right is a continuous curve, but the left shows a discontinuity when the strength is increased to 34 and the duration reduced to 0'0046 second. With smaller durations the strength remains constant and does not rise again until the duration is in the neighbourhood of 0'0004 second. Fig. 9 shows the curve for the left tibialis anticus with the electrode at a lower level. The curve rises gradually until the duration is reduced to 0'064 second and then remains constant at a strength of 14 until the duration is in the neighbourhood of 0'0004 second, after which it rises steeply.

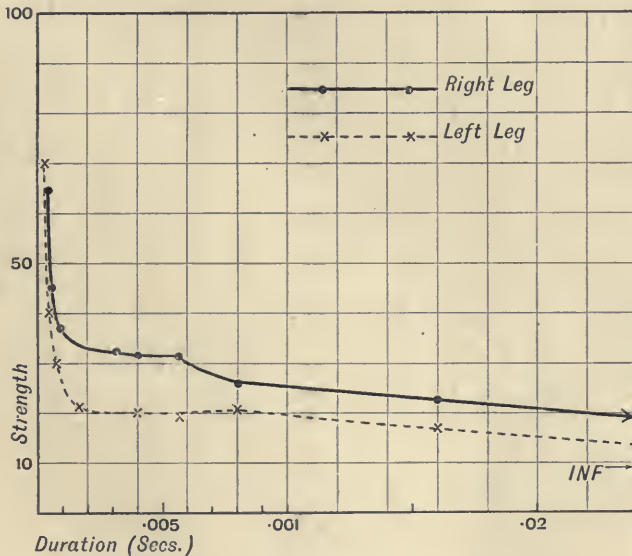


FIG. 10.—Toxic polyneuritis, recovering.

Case 8.—The patient had an attack of toxic polyneuritis of unknown origin in August, 1915. To begin with, both arms and legs were paralysed, but when he was examined he was recovering rapidly, had fair voluntary power in the arms and could walk for a short distance unaided. In spite of this the leg muscles showed no response to strong faradic currents and gave the typical reaction of degeneration with galvanic currents. The curves for the tibialis anticus on either side are shown in fig. 10. The curve for the right leg is an unbroken line and that for the left is interrupted. Both show a discontinuity, that on the left occurring when the strength is 20 and that on the right when the strength is 31.

Case 9.—The patient was shot through the right thigh in May, 1915. Immediately after the injury the leg was completely paralysed below the knee and there was complete loss of sensation over the area supplied by the sciatic. There was some return of voluntary power in the calf muscles in September, but the tibialis anticus was still paralysed. Its reaction to faradism was not determined. The strength-duration curve was determined on September 24 and again on October 7. At the first determination the current strength was not increased above 20; below this strength the curve is continuous and the chronaxie is 0.004 second. Fig. 11 shows the curve on October 7. There is a discontinuity at a strength of 24 and a duration of 0.0024 second. The lower part of the curve agrees in all respects with that determined on September 24.

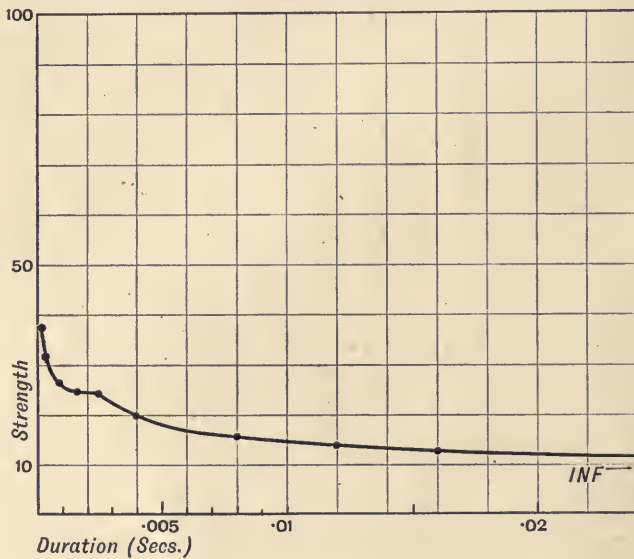


FIG. 11.—Incomplete sciatic injury, recovering.

A study of figs. 6 to 11 shows that there are certain common features in the strength-duration curves of all the muscles which gave evidence of recovery. In every case the curve is discontinuous and appears to be composed of two curves of the same form but with very different time-constants. The lower curve rises gradually at long durations; the upper starts from a higher base-line and does not begin to rise until the duration is very short. The point of intersection of the two curves varies widely, but it would appear from figs. 6 and 7 that it occurs at weaker strengths and longer durations as the condition of the paralysed muscle improves. If the time constants of these curves are

determined, it is clear that the upper curve has a short chronaxie which approximates closely with that for healthy muscle with intact nerve supply. In fact, the only point of difference between the curve for healthy muscle and the upper portion of these complex curves lies in the greater current strength needed in the case of the incompletely recovered muscle. Again, the lower half of the complex curve is very much like the curves for completely denervated muscle. The chronaxie of this part of the curve is certainly much more variable than the

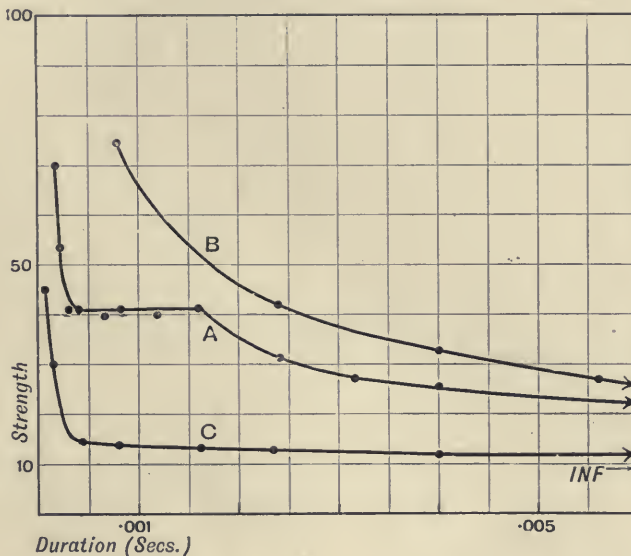


FIG. 12.—A, tibialis anticus recovering after poliomyelitis; B, tibialis anticus after complete degeneration of the sciatic; C, tibialis anticus with intact nerve supply.

chronaxie after division of the sciatic, but the figures are of the same order in both cases. A good example of this agreement is shown in fig. 12. In this figure the curve marked A is that for the right tibialis anticus in Case 6 (fig. 7 on a larger scale), B is a typical curve for denervated muscle (Case 1, fig. 4), and C is a curve for muscle with intact nerve supply. If the curve C could be made to rise from a higher base-line it is easy to see how the complex curve might be produced by a combination of the curve for intact with that for denervated muscle. There is certainly no sign of any gradual transformation of the curve for denervated muscle into that for healthy muscle, and this holds good for every case investigated.

INTERPRETATION OF RESULTS.

We have seen that in muscle with intact nerve supply and in denervated muscle the strength-duration curve is of a constant form, but that the time-constant is much greater in the case of denervated muscle than it is in intact muscle. Further, the results obtained on muscles which are recovering from incomplete nerve lesions make it clear that the slow curve characteristic of denervated muscle does not return gradually and without any discontinuity until it approximates to that for intact muscle. Instead of this, the curve for recovering muscle is complex and is always made up of two distinct curves, of which the slower corresponds more or less with that for denervated muscle and the more rapid with that for intact muscle. In the earlier stages of recovery the more rapid curve does not appear until the current strength is several times the minimal value. As recovery progresses the rapid curve becomes evident with weaker and weaker current strengths, until eventually it would seem to oust the slower curve altogether.

This result is of very great importance, for it shows that during recovery the current takes effect upon two distinct excitable mechanisms with very different time constants. At first sight it might seem possible to explain this on the assumption that the current affected two groups of muscle-fibres in different states of recovery. In poliomyelitis the different fibres of a paralysed muscle do not always recover at the same rate, and a part of the muscle may have voluntary power and response to faradism while the rest is completely paralysed and responds to galvanism only. These fibres might be so intimately mixed that it would be impossible to distinguish one set from the other by mere palpation. Consequently the strength-duration curve might be composite because it was made up of curves for several sets of muscle-fibres in different stages of recovery. However, if this were the case we should expect to find not one discontinuity in the curve but several. In fact, there would be as many discontinuities as there were different stages of recovery in the fibres under investigation. Moreover, there would certainly be curves in which the time-constant had a value intermediate between that for denervated muscle and that for muscle with intact nerve supply. Neither of these possibilities is realized in figs. 6 to 11. The only other possible explanation is that the mechanism upon which the current takes effect in muscle with intact nerve supply is quite distinct from that in denervated muscle, and that the great

difference in the time-factor in the two cases is not due simply to an alteration in the conditions of one and the same mechanism. On this hypothesis the recovery of the muscle is shown by the appearance of the mechanism characteristic of normal muscle in addition to the mechanism characteristic of denervated muscle. In the earlier stages of recovery the former mechanism needs a much stronger current to excite it than does the latter, but as recovery progresses the rapid mechanism becomes more and more excitable, until eventually it replaces the slower mechanism altogether.

It is not difficult to find a satisfactory explanation of the nature of these two mechanisms. In the frog, Lucas and Lapicque have shown that the nerve-fibres in the trunk of the sciatic and the nerve-fibres in the substance of the sartorius and gastrocnemius react to much more rapid currents than do the muscle-fibres excited directly. Now the great difference between normal muscle and denervated muscle lies in the fact that the former possesses healthy nerve-fibres running in the substance of the muscle, whereas the latter does not. Evidently in normal muscles there are two distinct excitable mechanisms, the nerve-fibre and the muscle-fibre, whereas in denervated muscle there is one mechanism alone. From the results obtained on the frog we should expect that the nerve-fibres would have a much shorter chronaxie than the muscle-fibres, and hence it is easy to see why the intact muscle gives a much shorter chronaxie than the denervated muscle.

During recovery from injury to the nerve, traumatic or toxic, the intramuscular nerve-fibres become active again, but at first we may suppose they are less excitable than usual. Under these circumstances we should expect to find a double curve, weak currents of long duration affecting the muscle-fibres directly, and strong currents of short duration affecting the intramuscular nerve-fibres. A process of this kind has been demonstrated experimentally in the frog's sartorius by Keith Lucas. The strength-duration curve of this muscle may be either a rapid curve characteristic of the nerve-fibres, or a slower curve characteristic of muscle, or else a double curve showing both components. The type of curve in any particular case depends on the relative excitability of the nerve- and muscle-fibres and on the distribution of the nerve-fibres in the neighbourhood of the electrodes. When the muscle is treated with curare the nerve-fibres gradually cease to transmit impulses to the muscles, and consequently the more rapid component of the curve disappears, to return again when the effect of the curare works off. Fig. 13 shows a double curve obtained by Lucas [8] from the

sartorius of the frog, and the resemblance between this and the curves for human muscle in figs. 6 to 11 is self-evident. So far, then, the explanation is simple enough. However, there are one or two points which call for further discussion. In the first place, the mechanism which has been excited by currents of short duration has been identified with the intramuscular nerve-fibre. If this is so, we should expect to obtain a curve with the same constants when the current is applied to the nerve-trunk instead of to the muscle itself. The average value of the chronaxie when the kathode is applied to the external popliteal

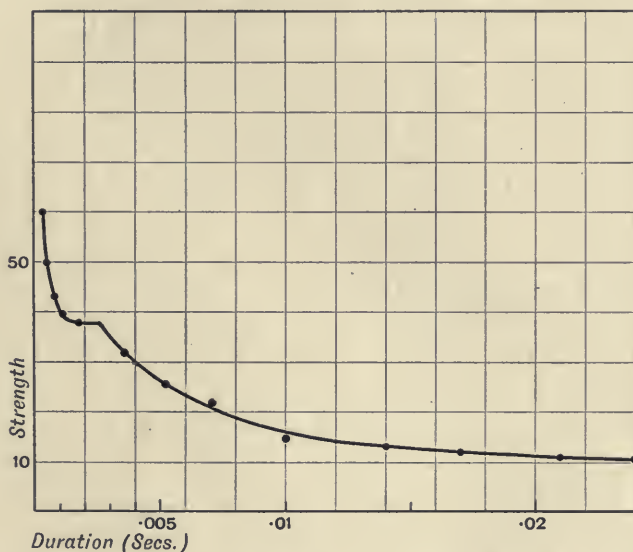


FIG. 13.—Frog's sartorius, showing stimulation of muscle-fibres (lower curve) and of intramuscular nerve-fibres (upper curve). (Keith Lucas).

worked out at 0.00025 second for four different cases. This is slightly longer than the value for the tibialis anticus. The difference may, of course, be due to experimental error.¹ However, there is another possible explanation which deserves mention. In the frog's muscle, in addition to the muscle- and nerve-fibres, Lucas has shown that there is a third excitable substance, which appears to correspond in distribution with the nerve-endings in the muscle. This substance has a shorter time-constant than the muscle-fibre, the chronaxie being 0.00017 second as

¹ Laugier (*loc. cit.*) finds that his *indice de vitesse* is the same for the nerve-trunk and for the muscle with intact nerve supply, see p. [31].

against 0.0005 second for the nerve. In the case of human muscles it is conceivable that a current applied to the muscle may excite a mechanism in the nerve-endings rather than in the intramuscular nerve, and this may explain the slower value of the chronaxie for the nerve-trunk. However, in the absence of more reliable figures, this cannot be insisted upon.

There is another possibility which must be discussed shortly. It is sometimes held that voluntary muscle is made up of two components—a fibrillar substance which reacts rapidly and a sarcoplasmic substance which reacts slowly. These two substances might, perhaps, be identified with the two excitable substances in human muscle, the fibrillar substance disappearing when the nerve degenerates. However, the idea has little or nothing in its favour. The independent existence of the fibrillar and the sarcoplasmic substances in mammalian muscle has never been proved, and there is nothing to show that they have the distinct properties with which they are credited. Furthermore, the electric reactions of the cold-blooded tissues are certainly due to the effect of the current on muscle-fibres and nerve-fibres, and it is difficult to believe that the reactions in human muscle are due to an entirely different mechanism. Much the same objection may be brought against the view that the two excitable mechanisms are to be identified with the white and red fibres of the muscle. It is true that the existence of these two sets of fibres is not in doubt, and it is true also that the white fibres degenerate more rapidly than the red. Again, the white fibres give a brisker contraction when they are stimulated, and therefore they might well react to currents of shorter duration. In human muscle the two types of fibre are intimately mixed, and so we might expect to find evidence of two different constants in the strength-duration curve. However, we have seen that the chronaxie of the rapid component of the double curve is equal to or slightly shorter than that of the nerve-trunk itself. This in itself is very much against the suggestion that the rapid curve is due to the white muscle-fibres rather than the nerve-fibres or nerve-endings; for, setting aside the comparatively close agreement between the chronaxie of the rapid curve and that of the nerve, no other case is known in which a muscle-fibre has a time constant equal to or shorter than that of the nerve-fibre which supplies it. Moreover, if the short chronaxie were due to the white muscle-fibres, we should not expect it to disappear until the muscle showed definite signs of wasting or to reappear until the wasting began to improve. Consequently, we must revert to the idea that

the two mechanisms in question are the muscle-fibre and the nerve-fibre.

A further point of interest concerns the value of the chronaxie for denervated muscle. After complete section of the sciatic the chronaxie always lay between 0·013 second and 0·009 second, and it has been suggested that this value is characteristic of muscle-fibre excited directly. It is naturally impossible to verify this by direct experiment on a human subject, as the effect of the nerve-fibres would have to be eliminated by curare or some such means. In the frog the chronaxie for muscle-fibre is about 0·007 second at 15° C., although we might naturally expect it to be longer than that for the muscles of a warm-blooded animal. This suggests the possibility that the chronaxie for human muscle-fibre would be really shorter than 0·01 second if it could be measured when the fibre was in a healthy condition, and that after the nerve is destroyed the chronaxie becomes longer on account of the abnormal state of the muscle. This view is upheld by the fact that in Case 9, where the nerve injury was incomplete, the chronaxie of the slower component of the curve was 0·004 second, a value which is less than half the average for denervated muscle. In spite of this it seems, on the whole, more probable that the figure of 0·01 second is the average value for muscle-fibres, and that the short value in Case 9 is due to an individual peculiarity and not to the improved condition of the muscle. If this were not the case we should expect the chronaxie to become longer and longer with the lapse of time following section of the nerve. The figures in Table II show that this lengthening does not occur. Again, in Case 7 (poliomyelitis) the chronaxie of the lower part of the curve is 0·02 second, although there was some return of voluntary power in the muscle, and although the chronaxie for the other tibialis anticus, which did not show any sign of recovery, was only 0·016 second. Consequently, the restitution of functionally active nerve-fibres is certainly not followed by an immediate shortening of the chronaxie for muscle-fibres. This does not imply that the chronaxie for muscle does not become longer as the muscle wastes and becomes converted into fibrous tissue. The muscles examined in Table II had all been treated by massage and electricity, and they showed very little wasting; on the other hand, in a few cases of ulnar and median injuries, with marked wasting of the small muscles of the hand, the chronaxie appeared to be considerably longer, 0·025 second or 0·03 second at least. These results are only rough approximations, as the method is very uncertain when applied to small denervated muscles in close contact

with small healthy muscles. Still, no doubt the chronaxie of human muscle-fibre may vary from 0.004 second to 0.03 second, or longer according to the state of the tissue. The important fact remains that functional connexion with the central nervous system may be restored, although the chronaxie of the muscle-fibres is twice as long as the average value for denervated muscle. The precise bearing of this result will be seen in the following section.

The conclusions arrived at in the present section may be stated briefly as follows: In muscle with intact nerve supply there are two distinct mechanisms upon which an electric current may take effect. These mechanisms are: (a) the intramuscular nerve-fibres, and (b) the muscle-fibres themselves. The nerve-fibre responds to currents of much shorter duration than the muscle-fibre, and in healthy muscle the strength-duration curve is always continuous and characteristic of nerve-fibre alone. In muscle which is in process of recovery after a nerve lesion the curve is discontinuous and is made up of two simple curves, one with the short time constant characteristic of nerve and the other with the long time constant characteristic of muscle. After complete degeneration of the nerve the curve is continuous and has the long time-constant characteristic of muscle. The constant may vary with the condition of the muscle, but its precise value does not affect the possibility of reunion with the nerve.

THE BEARING OF THESE RESULTS ON DIAGNOSIS AND PROGNOSIS.

If we accept the foregoing interpretation of the changes which follow injuries to the nerve we can draw certain conclusions regarding the possibility of electrical testing in general without reference to any particular method. For instance, it is clear that after a lesion which has produced complete degeneration of the nerve-fibres the electric reactions of the muscle itself can give no information at all as to the state of the nerve at the site of the injury. All we can hope to decide is whether the muscle is or is not in a fit state to recover its voluntary power when the nerve-fibres have regenerated. We cannot tell whether the lesion is one which makes regeneration impossible and therefore demands operation, or whether regenerated fibres are already growing down towards the muscle. The present observations show that the condition of the muscle itself, as indicated by the time constant, is of no great importance. It may remain for long periods unchanged after the complete degeneration of the nerve, and voluntary power may

return although the constant is twice as long as that six months after complete section (Case 7). The all-important factor is the condition of the nerve at the site of injury, and this we cannot hope to determine by electrical methods.

The position is altered when there are some nerve-fibres peripheral to the lesion which retain or have regained their excitability to electric currents. The presence of these fibres may be detected from the complex nature of the strength-duration curve and the production of a response in the muscle to currents of very short duration. If these fibres become more and more easily excitable it is safe to assume that the condition of the nerve is improving. In such cases the determination of the electric constants would show that the prognosis was favourable. However, these determinations would be of value only in those cases in which the possibility of recovery could not be deduced by simpler methods. For instance, if there is any return of voluntary power in the muscle there is clearly no need of an electrical examination to tell us that some of the nerve-fibres have regained their function. In three out of four of the cases of commencing recovery which were examined by the present method the return of a slight degree of voluntary power appeared to coincide with the reappearance of the curve with the short time-constant, and therefore with the reappearance of nerve-fibres which would respond to stimulation by electricity. In the fourth case (gunshot wound of the right thigh, Case 9) the strength-duration curve showed that some of the nerve-fibres could be excited electrically although there was no return of voluntary power in the *tibialis anticus*. Even so, the electric constants were not needed to show that the nerve was recovering, as there was already a considerable return of power in the calf muscles. Nevertheless, in so far as its history is concerned, the case is typical of a large number of incomplete nerve injuries caused by gunshot wounds, in which the paralysis clears up without operation, and much more rapidly than it should do if the nerve-fibres below the site of injury had degenerated completely. In these cases it is evident that the nerve-fibres below the injury must be still in some kind of trophic connexion with the motor cells in the cord, though they are unable to transmit impulses from the central nervous system to the muscle. Unfortunately, Case 9 was the only one of this class of injury which could be investigated by the present method, but it is not unreasonable to suppose that most if not all of them would agree with it in showing evidence of nerve-fibres peripheral to the lesion and yet capable of responding to electric stimuli. If so, the determination of the

strength-duration curve would give valuable evidence of the likelihood of recovery. When the curve does not show the characteristic discontinuity, we can only say that the nerve-fibres peripheral to the injury are inexcitable and that the possibility of recovery must remain in doubt. In such a case we may say with certainty that there is no method of electrical testing which will help to solve the question, since the current takes effect on the muscle-fibres alone, and the state of the muscle-fibres gives no indication of the state of the nerve.

In conclusion, we may say that a certain prognosis can be given only in those cases in which the nerve-fibres peripheral to the injury retain some measure of excitability. The presence of such fibres is shown by the complex type of strength-duration curve and the efficacy of currents of very short duration. How far their presence may be detected by the simpler methods of testing in vogue at present is a question which will be discussed in the following section.

The value of these results in diagnosis is another matter. To a certain extent any method of diagnosis which gives additional information as to the state of a diseased tissue must be counted of value, even though the information has no direct bearing on the treatment and prognosis of the case. The strength-duration curve gives definite information as to the state of the excitable mechanisms in nerve- and muscle-fibre, and this information may be expressed in a quantitative form. Furthermore Lapique, Keith Lucas and A. V. Hill have put forward theories as to the nature of electric excitation in which the constants of the strength-duration curve are given definite physical interpretations. These theories are based on Nernst's [11] original hypothesis that, in order to excite, the current must bring about a certain concentration of ions at the surface of a semi-permeable membrane in a substance of the fibre. Thus in Hill's theory the constants of the curve enable us to tell the charge on the ions, their rate of diffusion, the distance separating the membranes at which they take effect and the degree of concentration which must be attained in a given time for excitation to take place. These may be calculated as readily in the case of human excitable tissues as in those of the frog, and in this way it should be possible to relate a change in the condition of the muscle to a change in the diffusibility of the effective ions or the degree of concentration which must be attained at the membranes, &c. No attempt has been made to treat the present results in this way, because they are too few for such an elaboration and because the present theories of excitation are admittedly incomplete and in need of

alteration. For the present it must suffice to point out the possibilities of exact diagnosis which might be made on these lines.

PRESENT METHODS OF ELECTRICAL TESTING.

We have seen that the most important function of electrical testing is to determine the presence or absence of excitable nerve-fibres peripheral to the damaged area. If these fibres are present some weeks after the injury, the prognosis is good, and recovery may take place without operation. If they are absent, the prognosis is uncertain, but there is evidently no need to delay operation. It follows that the different methods of electrical testing must be valued according to their ability to detect these fibres. When the complete strength-duration curve is determined, the presence of active fibres is shown by the complex type of curve and the response to currents of very short duration. A current of 0.0004 second will excite nerve-fibres if it is strong enough, but it will not excite muscle-fibres, however strong it may be. So if we could always use a current of this duration and of variable strength there would be no need to determine the full curve. It remains to be seen how far this may be done with the methods in use at present.

(1) *The faradic and galvanic current.*—At first sight it might appear that the ordinary method of testing with the induction coil would be accurate enough, since the faradic current is of such a duration that it will excite nerve- but not muscle-fibre. However, it is evidently not at all suited to detect the presence of nerve-fibres if these are relatively inexcitable. It is well known that a muscle may regain some degree of voluntary power long before it shows any response to faradism, and in such a muscle there must be some functionally active nerve-fibres. Such a condition was found in all the cases of incomplete recovery described in this paper. The explanation of this state of affairs may be seen from fig. 7. In this case both legs had some return of voluntary power and the left tibialis anticus reacted slightly to faradism, whereas the right did not react at all. The strength-duration curves show that active nerve-fibres are present in both muscles, but in the right leg the current must have a strength of 40 if it is to affect the nerve, whereas in the left it need not be stronger than 29. With a short duration it is quite possible to employ a constant current of strength 40 or more without causing much pain, because the whole of the current is effective in stimulating the tissue. However, a faradic current of equal stimulating effect would be far too painful, because the

useful part of the current is only that fraction of the discharge when the electromotive force is at or near its maximum, and the remainder adds to the pain without taking any effect on the excitable tissue. Consequently the right tibialis anticus was put down as inactive to faradism because it was inactive to faradic currents of a strength which could be borne by the patient without an anæsthetic. Presumably the same holds good for every case in which there is voluntary power but no response to faradism. The nerve-fibres need a strong current to excite them, and a faradic current of this strength cannot be tolerated because of the pain it would cause.

(2) *The condenser method.*—This is clearly superior to the induction coil method because it is possible to select the duration of the discharge as well as the strength. Indeed, with some elaboration it would be possible to map out the full strength-duration curve with a series of condensers of different capacities. The discharge is more painful than that of a constant current, because the electromotive force falls off rapidly and the latter half of the discharge is useless. The duration of the discharge depends on the total resistance in the circuit as well as on the capacity of the condenser, but for practical purposes the difference in the resistance of two similar limbs is not great enough to matter. Consequently, it should be quite possible to select a capacity which would affect nerve-fibres without affecting muscle and to use this for detecting the presence of active nerve-fibres in incomplete lesions. It would be necessary to have some means of varying the strength of the discharge, or else to use a discharge so strong that there would be no chance of missing relatively inexcitable nerve-fibres.

The ordinary method of using condensers gives information of very doubtful value. If the muscle will respond to discharges of very short duration—0.05 mf. or less—we may safely infer that the nerve contains active fibres; but if a longer discharge is necessary, its precise value tells us nothing unless we know also the strength of the discharge relative to the strength required when the duration is infinite. If we do not know this, we cannot fix even one point in the strength-duration curve, and a change in the least capacity required to excite might be due to nothing more important than a change in the general excitability of the tissue brought about by increased skin resistance or excess of fluid in the subcutaneous tissues.

Consequently, there is nothing to be gained by stating the fact that a muscle responds to the discharge of a condenser of, say, 1 mf. capacity, unless we can add that the strength required must be a

definite multiple of that required at infinite duration. Without this information it is clearly quite impossible to determine the constants of the tissue.

(3) *Laugier's* [5] *method*.—This amounts to an attempt to determine the constants of the strength-duration curve by means of two stimuli of different duration. These are furnished by the make and break shocks of an induction coil, since the durations of these shocks are fixed quantities depending on the dimensions of the coil, and the duration at make is several times as long as that at break. A comparison of the strengths of current required to excite at make and at break gives a quantity which Laugier calls the *indice de vitesse* of the tissue, and which is proportional to the slope of the strength-duration curve between the points corresponding to the durations of the make and break shocks. The index is not affected by simple changes in the excitability of the tissue, and a change in the index always denotes a change in the slope of the curve. The method is ingenious and simple to apply, but it is based on a misconception of the changes which take place when the nerve is damaged. If the rapid curve characteristic of normal muscle were transformed gradually and without discontinuity into the slow curve of denervated muscle, and vice versa, the slope of the curve between two fixed points should give all the information necessary to determine the condition of the tissue. However, we have seen that the transition is abrupt and that the two curves are quite distinct, the rapid curve becoming more and more prominent as the process of recovery advances. When the curve is discontinuous, the slope between two fixed points will depend on the position of these points in relation to the discontinuity, and although a change in the slope will imply a change in the complex curve, the notion of the *indice de vitesse* loses its simplicity and is no longer a quantity definitely related to the constants of the tissue under examination.

Practically the method has the disadvantage that it cannot be applied to a muscle which has lost its excitability to faradic currents, since the stimuli are necessarily of very short duration. In any case it cannot be said to take the place of the complete determination of the strength-duration curve, since the double curve cannot be defined by two points only, whatever may be the durations corresponding to these points.

SUMMARY.

The curve which expresses the relation between the least strength and the least duration of the current required to excite has the same form for human tissues as it has for the tissues of cold-blooded animals. The time-constant of the curve is determined by the duration at which the current strength must be twice the minimal value. This duration is characteristic of the tissue examined, and it has been named the "chronaxie." In healthy muscle with intact nerve supply the chronaxie is very short, 0.00016 second on the average, and it is slightly longer when the electrode is applied over the nerve-trunk instead of to the muscle directly. When the nerve has degenerated the chronaxie is very much longer. Its average value is 0.011 second, and, in the case of the tibialis anticus at any rate, it shows surprisingly little variation with increased lapse of time following the injury. When the muscle is in process of recovery, the slow curve of denervated muscle does not pass gradually into the rapid curve of healthy muscle; instead of this, the first sign of recovery is marked by the appearance of a discontinuity in the strength-duration curve. With very strong currents the curve has the short time-constant characteristic of healthy muscle, but with weaker strengths a slower curve appears, and this has the long time-constant of denervated muscle. The production of these double curves shows that there are two distinct mechanisms upon which the current may take effect; only the slower mechanism is present in denervated muscle, and as recovery takes place the more rapid mechanism comes into play and eventually predominates, to the exclusion of the slower mechanism. Reasons are given for the belief that these two mechanisms are to be identified with the muscle-fibre and the nerve-fibre or nerve-ending. Thus the appearance of the discontinuity in the strength-duration curve and the response to currents of very short duration shows that there are some excitable nerve-fibres peripheral to the injury. This is to be expected in those cases of incomplete injury where the trophic influence of the nerve cells is not abolished, although impulses cannot pass from the central nervous system to the muscle. When the curve is continuous and has the slow chronaxie only, all that can be said is that there are no excitable nerve-fibres peripheral to the injury. The possibility of regeneration depends on the state of the nerve at the site of injury, and this cannot be determined electrically. The condition of the muscle is not of very great importance, for voluntary power may begin to return although the chronaxie of the muscle-fibres is twice as long as it is nine months after complete

degeneration of the nerve. It follows that the most important function of electrical testing is to decide whether there are any excitable nerve-fibres peripheral to the injury. If there are, and if they are becoming more excitable, then there is no need to operate; if not, we cannot tell whether the nerve will regenerate or not, and there is no reason to delay operation.

The different methods of testing in vogue at present give some information as to the presence or absence of these fibres. The method of condenser discharges is the most reliable, but the usual method needs several modifications; in particular, the strength of current must be a definite multiple of that required at infinite duration, otherwise a change in the general resistance of the limb, &c., may be mistaken for a change in the time constant of the muscle.

The present investigations were carried out on the military cases at the National Hospital for the Paralysed and Epileptic, Queen Square, and I am deeply indebted to the medical and surgical staff of the Hospital for allowing me to make use of these results.

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DISTURBANCES OF VISION FROM CEREBRAL LESIONS, WITH SPECIAL REFERENCE TO THE CORTICAL RE- PRESENTATION OF THE MACULA.¹

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IN our work in the base hospitals in France during the past eighteen months we have observed a very large number of cases in which vision was affected by the lesions of various portions of the optic system, but time and opportunity have not permitted a careful and complete examination of all. Consequently, in many cases of considerable clinical importance we possess only scanty and incomplete notes; but by selecting for thorough investigation a certain number of suitable cases we have been able to collect a group of facts that have an important bearing on the cerebral localization of vision, and more particularly on the representation of different regions of the retina in the cortex.

Owing to the conditions under which we have worked, most of our observations were necessarily made at a relatively early date after the infliction of the wound; we recognize that this fact makes possible the objection that, as our cases were mainly examined during the stage in which the effects of shock or diaschisis were still present, the visual defects we describe may have been due to functional disturbances rather than to localized injuries of the corresponding cortical areas or of their centripetal fibres: but if we can show that there is a constant relation between the probable site of the injury and the form of the visual defect, it is obvious that certain general conclusions at least will be justifiable.

The fact that most of our patients were investigated in the early stages also presented certain technical difficulties; as most were confined to bed a small hand perimeter had to be employed, but in some the observations were later controlled by a McHardy perimeter. We have

¹ Read before the Ophthalmological Section of the Royal Society of Medicine, March 22, 1916.

also employed a modification of Bjerrum's screen¹ to determine the exact relations of smaller defects. Further, as such patients tire easily and quickly, repeated examinations were often necessary. On the other hand, the fact that most of the wounds were recent has enabled us to make many interesting observations on the mode and rate of recovery of vision from different forms of injury.

Since the time of Munk, who from his experimental observations attempted to project the retina directly on to the cerebral cortex, the localization of visual function has excited much interest, but until relatively recently nothing was known of the exact limits of the visual area, or of the regional representation of the retina within it. Certain authors, and especially Henschen and J. S. Bolton, have, however, discovered pathological evidence that the visual area coincides with that cortical zone of special structure which is now generally known as the area striata (fig. 1). This is the area, distinguished by Gennari's line, which lies within and on both lips of the calcarine fissure and which, even in the higher races of mankind, but to a greater extent in the lower, extends to and around the pole of the occipital lobe. There is now considerable evidence, due chiefly to the work of Henschen, that the upper half of each retina is represented in the upper parts of these areas, and the lower in the lower walls and lips of the calcarine fissures; destruction of the upper portion of the area striata on one side would consequently produce a lower quadrantic homonymous hemianopia in the opposite halves of the visual fields, and vice versa.

On the other hand, nothing is definitely known on the correspondence between various concentric zones of the retina and the different segments of the area striata.

The question of the cortical representation of the macula has for a

¹ A description of this modification may be useful, especially to those engaged in similar work. A large sheet of paper (double foolscap), covered with black cloth, is placed on a flat board and both are pinned to it. A small drawing-pin serves as a fixation point. The test object is carried on the blunt end of a steel pin, about $\frac{1}{2}$ cm. in length, which is fixed transversely across the end of a dark metal rod, so that its point projects about 1 mm. on the opposite side. The test object thus fixed on the end of the rod is moved slowly from the blind region along the screen until the patient sees it; then the carrier is simply pressed against the board so that the point of the pin penetrates the cloth and marks the paper beneath it.

A large number of observations are taken. If the distance of the fixation point from the eye is known—we generally use it at a distance of 1 m.—the record thus obtained can be transferred to an ordinary or to a special perimeter chart.

One advantage of this method is that as there are no lines or marks on the screen which can influence the patient or the observer, the records obtained by it are absolutely unbiassed.

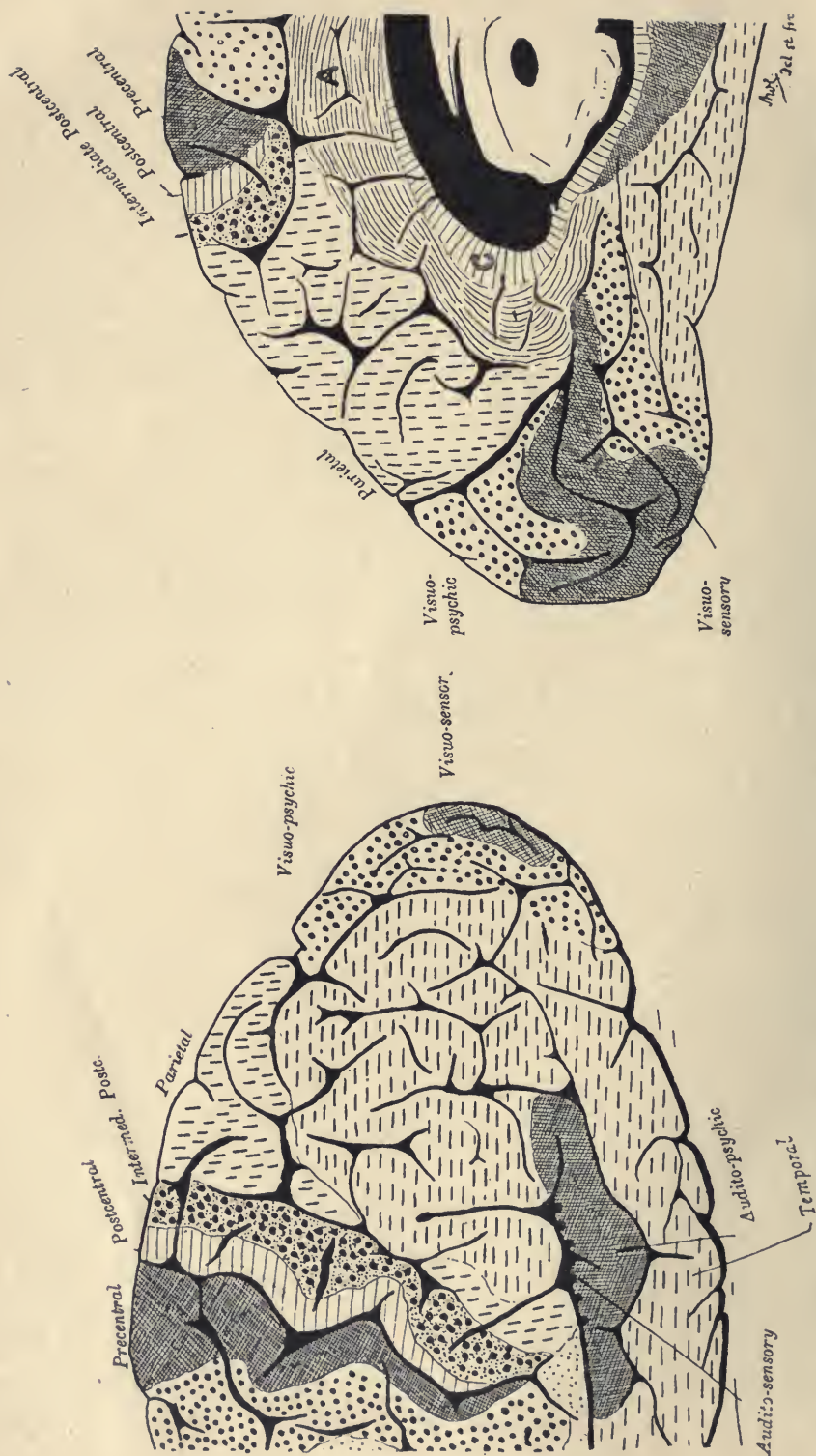


FIG. 1.—To show the superficial distribution of the area striata (visuo-sensory) on the mesial and lateral surfaces of the hemisphere (Campbell).

long time excited much interest. Owing to the fact that in the majority of those cases of homonymous hemianopia due to vascular lesions which are seen in civil practice, vision is unaffected for a distance of 2° to 10° to the blind side of the fixation point, it was for a time generally assumed that each macular area is represented in both hemispheres; this hypothesis was apparently supported by the anatomical observation that at the chiasma branches of the macular fibres from each eye pass into each optic tract. But the fact that in bilateral hemianopias due to lesions of both occipital lobes central vision often persists confuted this view, and gave origin to the hypothesis that the macular centre must lie outside the area striata, or may not indeed be locally represented in any part of the cortex (von Monakow).

Others have attempted to explain the macular escape in hemianopia by assuming that the two cortical macular centres are connected by callosal commissural fibres (Lenz, Heine), or by the hypothesis that the physiologically more highly developed macular impulses pass more easily through an incomplete block (Ronne).

Within recent years, however, many attempts have been made to determine a localized macular centre in the cortex. Henschen, for instance, first assumed that the macular focus lies in the anterior portion of the calcarine cortex, and later that it extends along the whole floor of the calcarine fissure. J. S. Bolton, too, has recently assumed that the "calcarine core" of the visual cortex is the anatomical basis for macular vision. On the other hand, Inouye, in his excellent monograph on the visual disturbances observed after gunshot injuries of the occipital lobes inflicted in the Russo-Japanese War, brings evidence showing that the macular centre must lie towards the pole of the occipital lobe; while Lenz, in a general review, concludes that though certain published cases indicate its localization anteriorly in the calcarine cortex, more are in favour of its representation posteriorly in this region.

Our own observations will bear on all these points. It must be recognized, however, that there are difficulties in determining the exact site of the essential lesion in the optic system, and even when the position of the injury is exactly known, it is not always easy to correlate the visual disturbance with it. This is largely due to the fact that, as the optic radiations in sweeping backwards along the outer side of, and especially behind, the posterior horn of the ventricle, lie in relatively close relation to the area striata, either these or the cortex, or both, may be affected by the one lesion, and consequently the exact cause of the visual disturbance may be uncertain. Since,

however, the fibres of the radiations that reach the most posterior part of the pole are probably distributed only to the most posterior part of the calcarine cortex, visual defects associated with their injury here may bear directly on the question of cortical localization. On the other hand, an extensive lesion in the middle or anterior portion of the calcarine cortex may involve any or all of the fibres of the radiations, and the associated visual defects may give us no clue to localization.

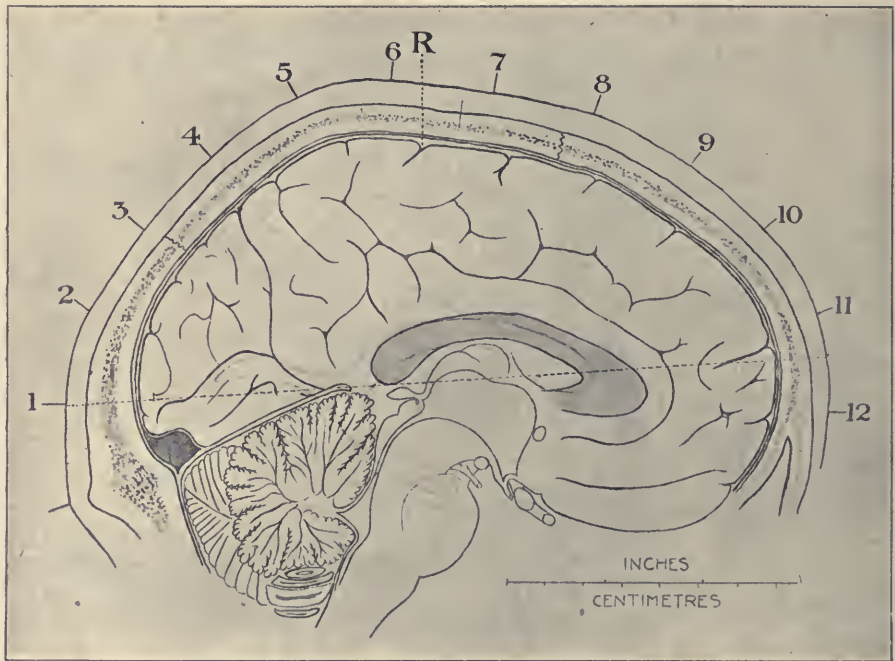


FIG. 2 — Mesial sagittal section of an average-sized head (distance between nasion andinion $13\frac{1}{2}$ in., or 34 cm.) to show the relation of the calcarine fissure to the inion. The lines vertical to the surface of the figure indicate the distance of each point from the inion in inches, measured along the scalp in the middle line of the head.

There is, however, considerable evidence to show that the fibres in the radiations are to some extent arranged according to their destination in the area striata. Otherwise many published records would be unintelligible.

The injuries in our cases include penetrating and perforating wounds of the cranium by rifle bullets, shell fragments and shrapnel, as well as local concussions and depressed fractures.

The portions of the brain injured can be approximately determined when there is a depressed fracture or a penetrating wound of the skull by noting its relation to certain fixed points, as the inion, supplemented by a stereoscopic X-ray examination. If the relations of the calcarine fissure and of the area striata to this fixed point are approximately

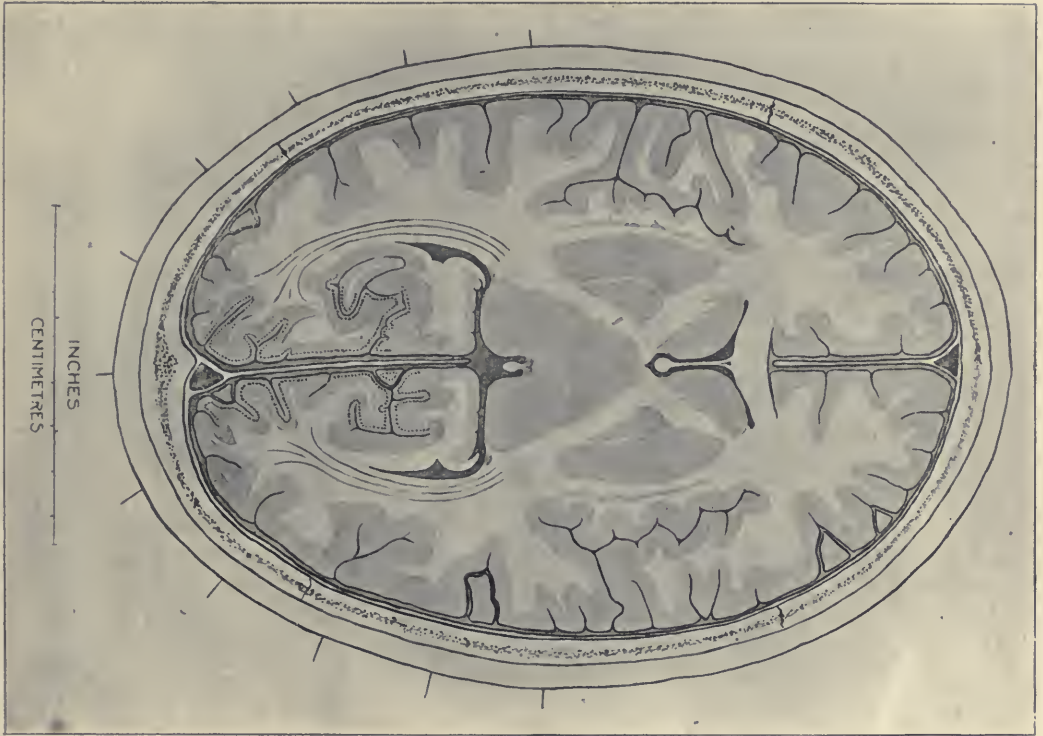


FIG. 3.—A horizontal section through an average-sized head, taken 1 in. above the tip of the inion and 2 in. above the nasion, in the plane represented by the broken line in fig. 2, to show the relations of the area striata. This is indicated by a broken line in the occipital cortex. The marks on the surface of the scalp represent inches measured in this plane from the middle line posteriorly.

constant, as we have found them to be (fig. 2), the position of the cerebral injury can be often fixed within relatively close limits, and if the anatomical relations of the whole of the visual cortex, as seen in both sagittal and horizontal sections (fig. 3), are also known, then in the case of traversing bullets and fragments of shell, the entrance and exit wounds of which can be measured from a fixed point, the track of the missile can be calculated, since experience has shown

that bullets usually take a straight course between the entrance and exit wounds. It must be remembered, however, that the amount of destruction produced by such missiles may vary much. In many of the cases we have been also able to determine the approximate site and extent of the cerebral injury during operation, and in a few cases we have been able also to verify it by *post-mortem* examination. But though the exact localization of the lesion may appear to be indefinite, the consensus of evidence will be, we believe, sufficiently strong to justify certain positive conclusions.

QUADRANTIC DEFECT IN THE VISUAL FIELDS.

We have been able to observe a certain number of cases of so-called quadrant ic hemianopia, and will first deal with them, selecting those that throw most light on the question of the cortical representation of the upper or of the lower quadrants of the retina:—

Case 1.—Lieutenant C. was wounded February 26, 1915, by a fragment of shell. He was unconscious for a short time, and afterwards had much headache, and found his sight was affected. He was operated upon next day in a casualty clearing station, when pieces of depressed bone were removed, and was sent to the base a week later.

Wound.—There was then an oval open wound surrounded by a flap incision; its centre was $3\frac{1}{2}$ in. (9 cm.) above and 1 in. (2.5 cm.) to the right of theinion, and from here a track, closed at its lower end, but open for about $\frac{3}{4}$ in. (2 cm.), passed horizontally forwards into the brain. He had then loss of vision in the lower left quadrants which came to within 5° of the fixation point. He presented no other abnormal symptoms (fig. 4). His wound healed rapidly, and he was evacuated to England.

It is obvious that in this case the wound, which was of considerable size, lay above the right calcarine fissure.

Case 2.—Staff-Serjeant M., 20,175, was wounded by a piece of shell-casing on May 23, 1915. He was unconscious for a short time, and later had very severe headache and vomiting. He also found his vision seriously affected at first. When he arrived at the base next day there was a large wound, the centre of which lay $2\frac{1}{2}$ in. (6.5 cm.) above the inion and $\frac{1}{4}$ in. (0.5 cm.) to the right of the middle line. An X-ray plate showed fragments of bone and a small piece of metal driven into the brain, directly forwards, to a considerable depth; these were removed with some septic and disintegrated brain, and the track drained. He made an uninterrupted recovery and was transferred to England about three weeks later. While under observation he had a complete loss of vision in the lower left quadrants and slight limitation in the periphery of the left upper quadrants (fig. 5).

In this case, too, in which a considerable amount of brain was probably damaged, the lesion lay above the level of the right calcarine fissure.

Case 3.—Lance-Corporal M., 4,940, was wounded by a bullet on March 24, 1915. He was not unconscious, but had severe frontal headache and vomiting for some days. He was completely blind at first, but on the fifth day was able to recognize light to the right of the fixation point.

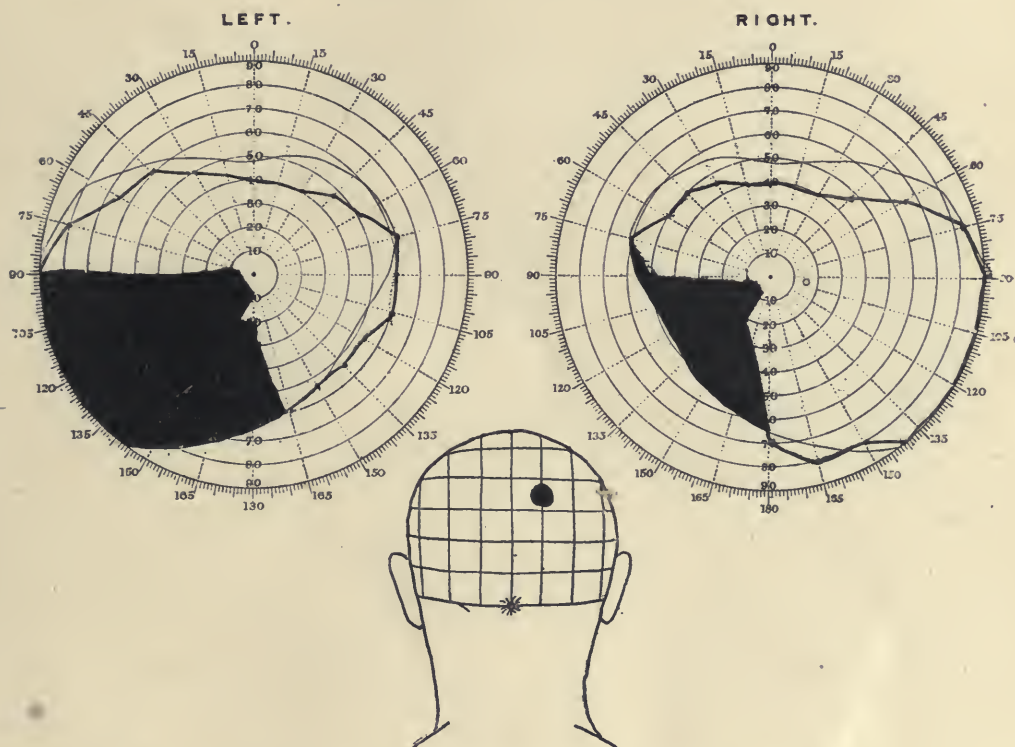


FIG. 4.—In this and the following figures the position of the wound is represented approximately on a diagram of the back of the head. The horizontal lines on this represent the distance in inches of the plane in inches above the inion, the vertical the distance in inches from the middle line of the skull.

The wound, which was $1\frac{1}{2}$ in. (4 cm.) above the inion, extended across the middle line; it had been operated upon in a casualty clearing station, and depressed fragments of bone were removed. An X-ray examination later showed a defect in the skull, chiefly to the right, and a linear fracture running forwards to the right side. When seen at the base five days later he had distinct vision only immediately to the right of the fixation point, but on the seventh day had an almost full field in the right upper quadrant, but could recognize colours only by central vision. On the fifteenth day after the infliction of the wound there

was some further recovery in the lower right quadrant near the fixation point, and the colour fields in the seeing portion of the fields was almost full (fig. 6); on the left the blindness extended up to the fixation point.

In this case the lesion lay immediately above the posterior end of the calcarine fissures; it evidently produced considerable destruction in the right hemisphere, and probably affected only the upper portion of the calcarine cortex on the left.

LEFT

RIGHT

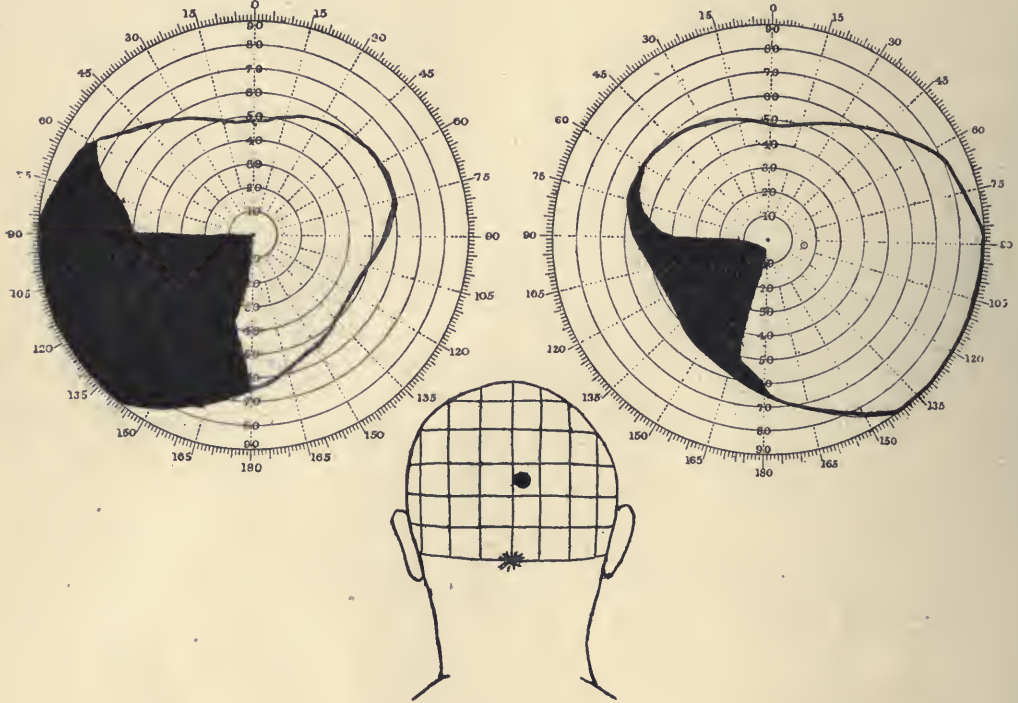


FIG. 5.

Case 4.—Private J., 13,613, was wounded about December 1, 1915, by a bullet. He was unconscious for some days, and, on regaining consciousness, found he was quite blind, but on the next day he could see to the right side. There was no paralysis, sensory disturbance, or reflex changes.

Wound.—The bullet entered in the right lower parietal region $2\frac{1}{2}$ in. (6.5 cm.) above and $1\frac{3}{4}$ in. (4.5 cm.) behind the upper margin of the attachment of the right auricle, and made its exit 2 in. (5 cm.) above the inion and $1\frac{3}{4}$ in. (4.5 cm.) to its left. On his arrival at the base, probably about a week later, small flaps were turned down around both wounds and some depressed fragments of bone removed from the entrance. He made an uneventful recovery. About three weeks after the infliction of the wound his visual fields were carefully examined with test objects 4 mm. in diameter, and it was found

that his vision was limited to the left upper quadrants. The blindness approached to within 3° of the fixation point (fig. 7).

In this case the bullet probably entered in the right angular gyrus, injured the upper part of the right optic radiations beneath it, and, assuming it had gone straight through the skull, it would have passed through the upper part of the right area striata and then entered the left hemisphere through the middle of the area striata, probably near the parieto-occipital fissure.

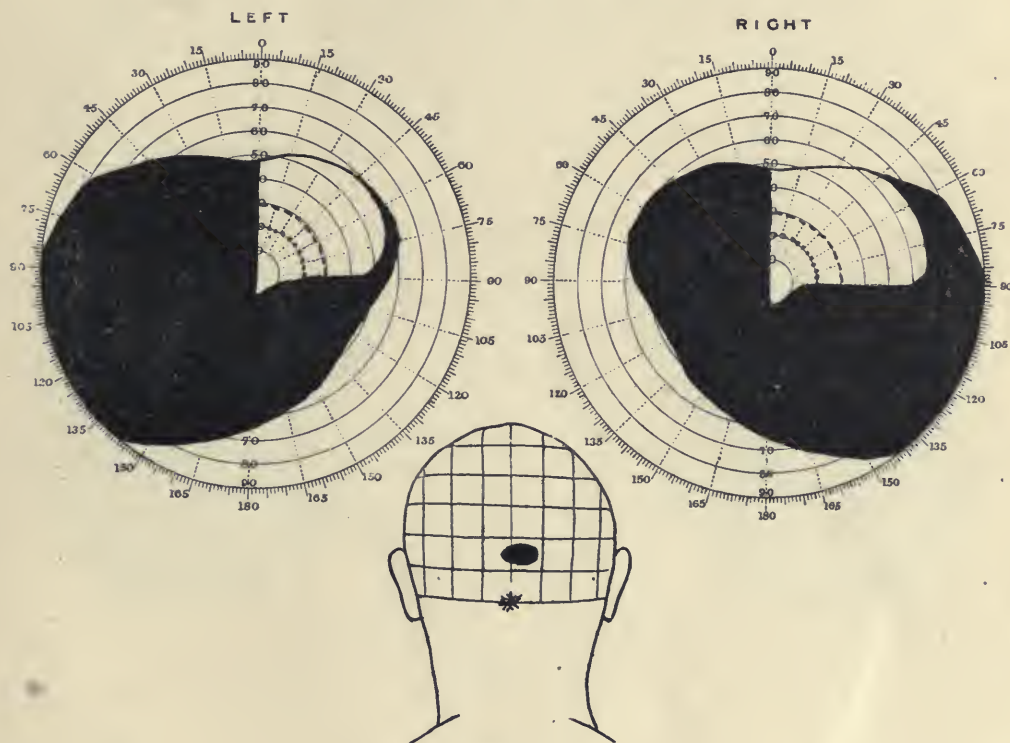


FIG. 6.

We have so far seen only one case of horizontal hemianopia in which the patient's state permitted a careful perimetric examination, but even in this patient there was in addition a superior paracentral scotoma.

Case 5.—Private P., 17,961, was wounded by a rifle bullet on September 25, 1915. He was unconscious for about twelve hours, and thereafter had severe headache and found his sight misty. He arrived at the base three days later.

Wound.—The entrance was a small puncture 3 in. (7.5 cm.) to the left of the middle point of the vertex, the exit being 1 in. (2.5 cm.) above and $1\frac{1}{2}$ in. (3.75 cm.) to the right of the inion. An X-ray examination showed a small entry wound through the skull with a few small fragments of bone driven in,

and a larger blown-out exit wound to the right of and about $1\frac{1}{2}$ in. (3.75 cm.) above theinion. There was then some general weakness of his right arm and of this side of his face, but his legs were equally strong, and the only changes in his reflexes were absence of the right arm-jerks and diminution of the right abdominal reflex. There was also considerable sensory disturbance of the cerebral type in his right upper limb, the appreciation of position, passive movement and form, and the discrimination of compass-points, being lost. The motor symptoms disappeared almost entirely while he was under observation, but some sensory disturbance persisted. His headache was relieved by

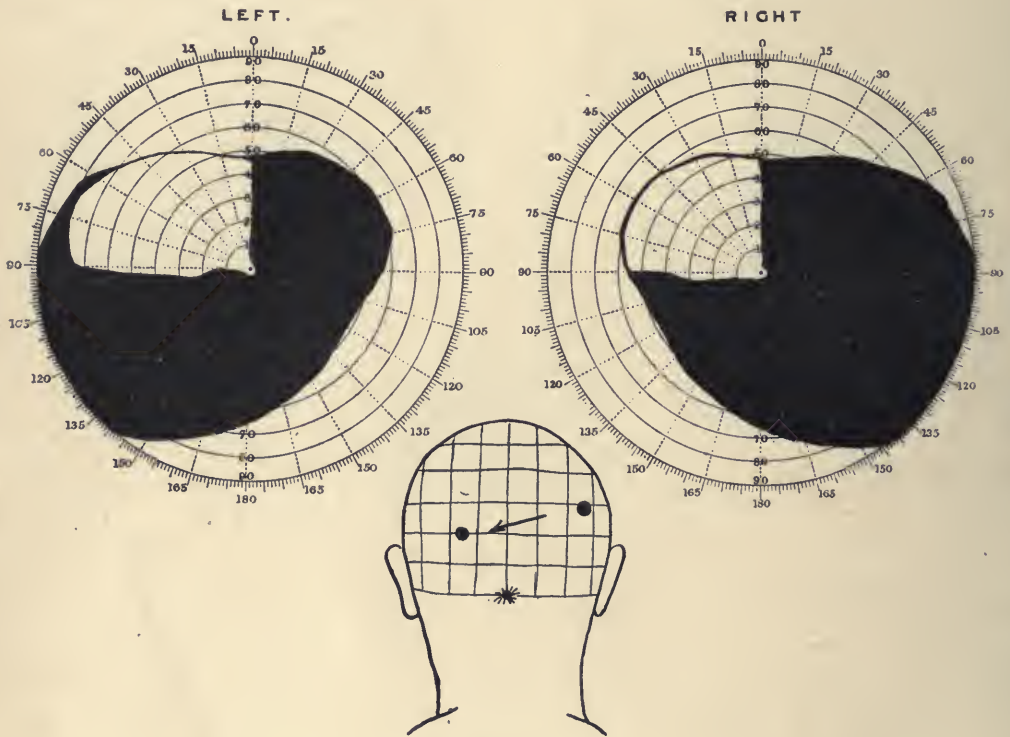


FIG. 7.

lumbar puncture and did not recur. His wounds healed rapidly. When he was first seen, four days after the infliction of the wound, central vision was defective, and he was unable to see below a horizontal line through his fixation point. On October 11, however, central vision was $\frac{6}{8}$ in each eye, and he easily read Jaeger 1, but there was obviously a scotoma to the left of and above the fixation point. A few days later, when he was able to leave his bed, his visual fields were taken carefully and a complete lower horizontal hemianopia, almost limited by a horizontal line through the fixation point was discovered. There was an absolute left superior paracentral scotoma which came

almost up to the fixation point (*see below*) and extended out to 10° (fig. 8). Colour vision was normal at the fixation point and in the superior quadrants, except in the position of the scotoma, where its loss was coterminous with that for white. He remained under observation for five weeks after the infliction of the wound, and during the last three weeks of this period the visual disturbances remained stationary.

In this case the bullet probably entered the left posterior central gyrus at about the level of the superior genu of the fissure of Rolando, passed obliquely backwards, downwards and inwards through this hemisphere in the neighbourhood of or through the upper portion of the sagittal strata, and, from the position of the exit wound, probably cut through the upper part of the right calcarine area and through its posterior extremity at the pole of the hemisphere.

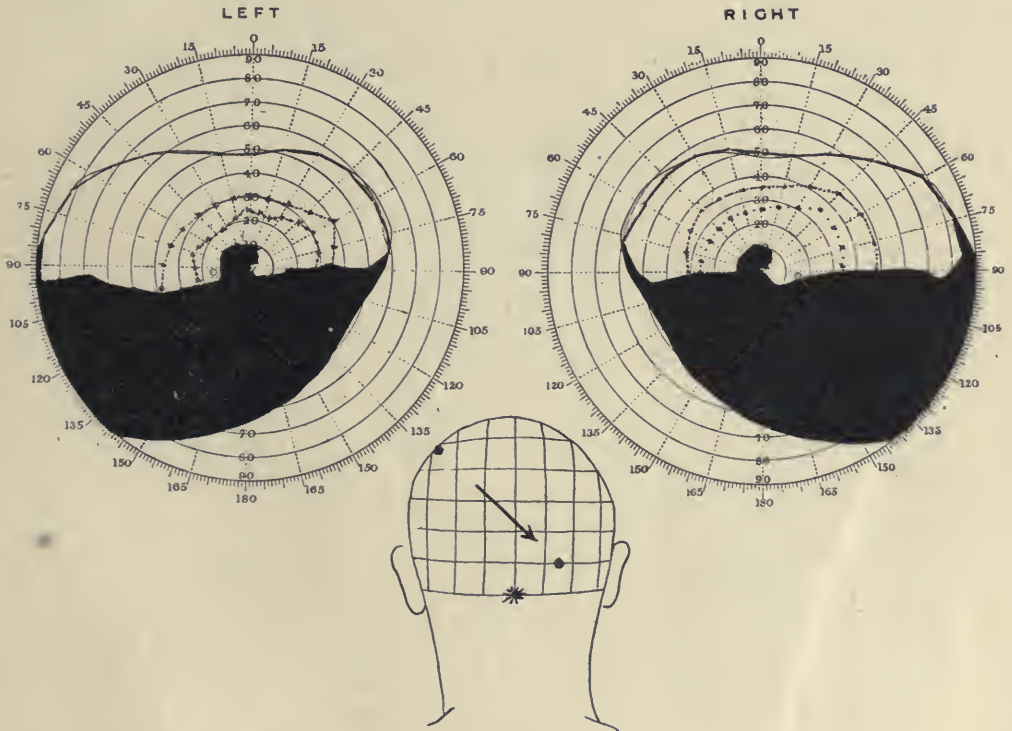


FIG. 8.

It will be noticed that in those cases where one quadrant only was affected it was always the lower quadrant of the visual field, that is, the sector which corresponds to the opposite superior quadrant of the retina, which was blind; this was so in all the cases in which we have observed complete or partial quadrantic blindness. Further, in all cases the

position of the injury or the course of the missile made it probable that the brain was damaged chiefly above the level of the calcarine fissure, and our cases consequently support Henschen's view, for which there is now much evidence, that the upper halves of the retinae are represented in the upper lips of the calcarine fissures. Inouye's observations on cases injured in the Russo-Japanese War point to the same conclusion.

The rarity of superior quadrantic hemianopia in gunshot injuries of the occipital region is striking; it is probably due to the fact that through-and-through or penetrating wounds in the inferior part of the area striata are liable to produce lesions in the cerebellum, which are notoriously very fatal. The fact that only the upper quadrants on one side escaped in Cases 3 and 4, in which the lesion on the opposite side probably lay above the level of the calcarine fissure, is evidence that the inferior portions of the retina are represented in the inferior parts of the area striata.

CENTRAL SCOTOMATA.

We have had the opportunity of seeing a considerable number of central and paracentral scotomata, and will describe here those cases which bear most definitely on the vexed question of the cortical representation of the macula.

Case 6.—Private F., 2,312, was wounded by a bullet on July 11, 1915. He was unconscious probably for two days, and later had severe headache and found his sight seriously affected.

Wound.—There was a glancing wound across the middle line just above the inion, the entrance being on the right side and slightly above it, the exit on the left and immediately below its level. An X-ray stereoscopic examination showed a grooving of the outer table of the skull at the upper margin of the inion and the depression of a large flake of the inner table on to the poles of both occipital lobes. He was first seen four days after the injury; vision was then much disturbed, but it was not possible to take his visual fields by the perimeter till a week later. Then a large absolute central scotoma, which extended all round the fixation point to about 15° , except below, where it came within the 10° circle, was found. In this area there was complete blindness to white and to colours, the test objects being 2 mm. square. The peripheral fields for both white and colours were unrestricted. (In this and in the following cases, in which central vision was affected, fixation was obtained by placing the tip of the patient's forefinger on the fixation point of the perimeter and making him gaze at it.) He remained under observation for three weeks after the injury; towards the end of this period vision improved to some extent, so

that there was complete blindness only in the upper left quadrants, while over the rest of the scotomatous area there was some, though indistinct, vision (fig. 9).

In this case it was only the tips of the occipital poles which were probably

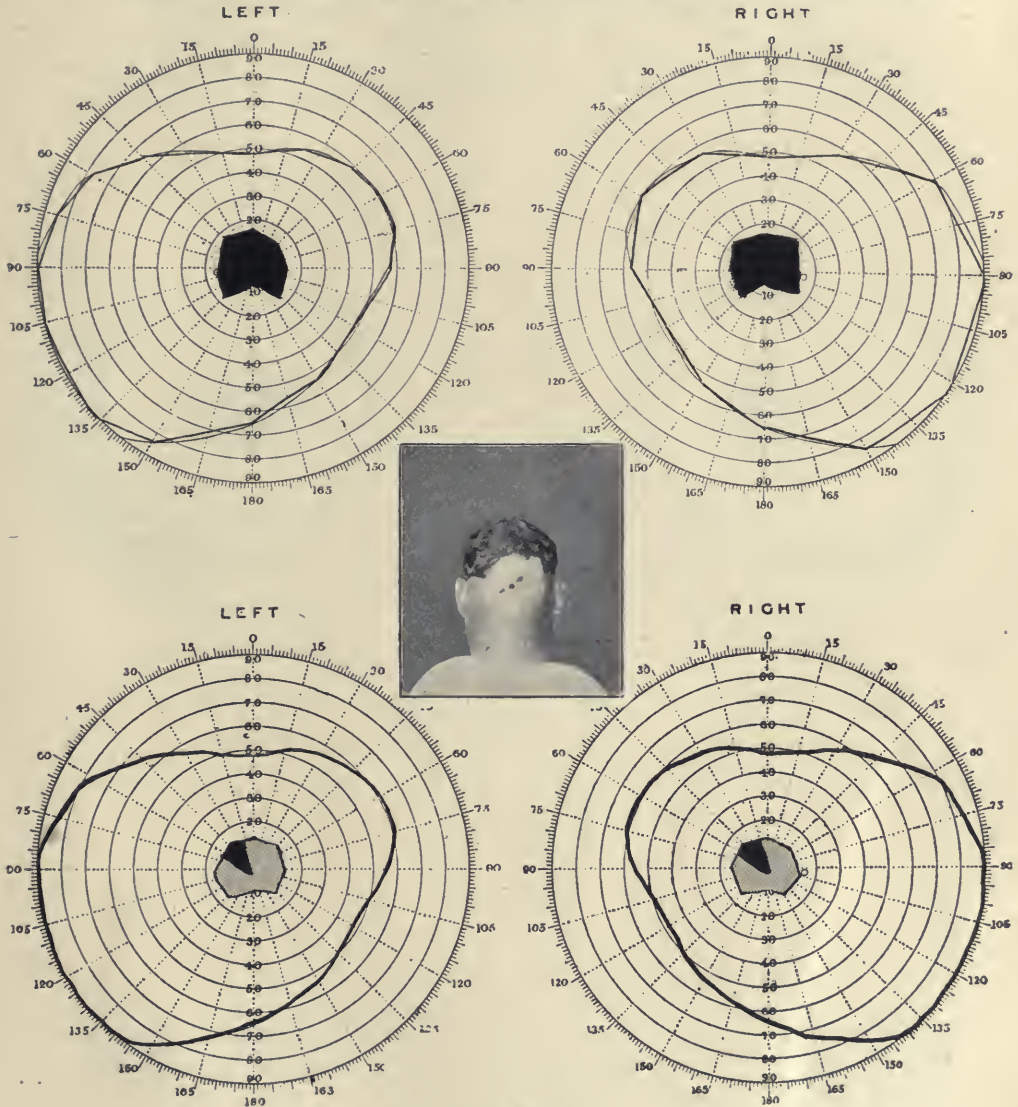


FIG. 9.

injured; they must have been bruised by the depressed portion of the inner table of the skull.

Case 7.—Private R., 1,629, arrived at a base hospital on March 7, 1915. He had been unconscious for some days and could give no history of his injury or of the operation which had been done at a casualty clearing station.

The *entrance wound* was 2 in. (5 cm.) to the left and $\frac{1}{2}$ in. (1.25 cm.) above the level of the inion, while the exit was 2 in. (5 cm.) to its right and 1 in. (2.5 cm.) above its level. There was a small bone defect beneath each wound, through which tense cerebral herniæ protruded. That under the entrance wound did not pulsate: When admitted he had much headache and papilloedema with swelling of 1.5D. to 2D. The right eye was astigmatic and had been amblyopic since infancy, and he had a slight convergent squint.

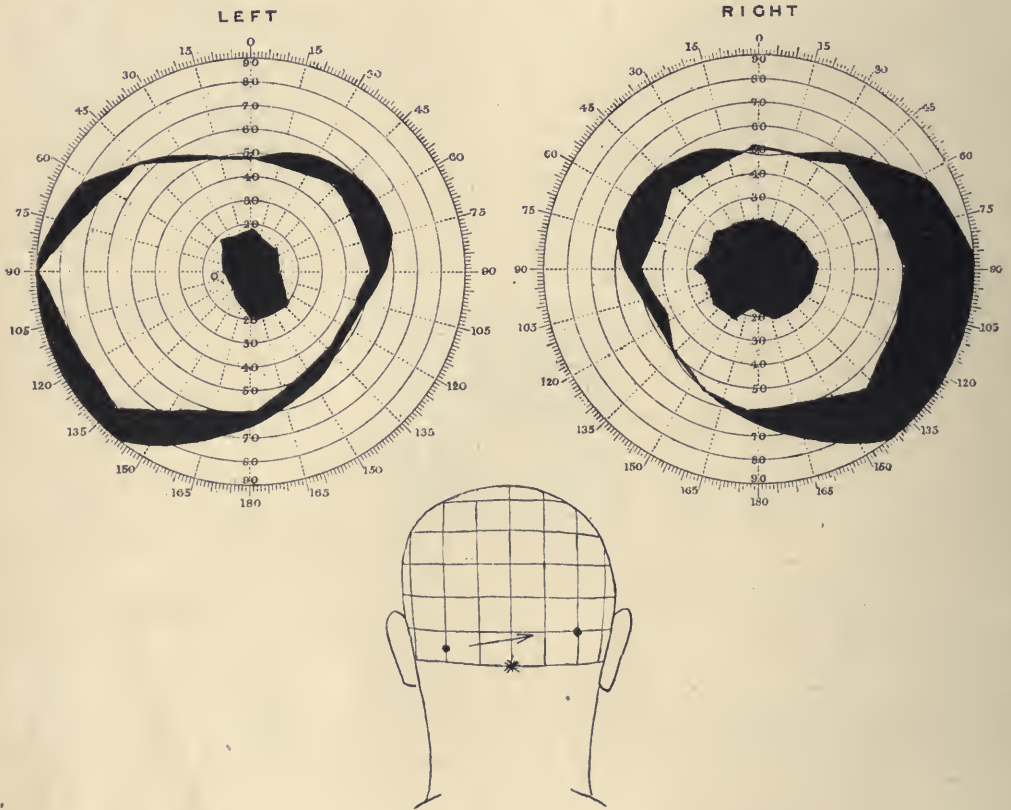


FIG. 10.

Apart from the visual disturbance there were no other symptoms of cerebral injury. His visual fields, taken about ten days after the infliction of the wound, showed a large central scotoma in each eye, which was somewhat more extensive in the right than in the left, and in the amblyopic eye there was also some peripheral contraction, which was probably due to want of attention (fig. 10). The scotomata were practically unaltered when his fields were taken again a few days later and remained so till he was transferred to England.

In this case the wounds were due to a bullet which had passed horizontally across the occipital poles at about the level of the posterior ends of the

calcarine fissures, and which must have consequently destroyed the posterior part of each area striata.

Case 8.—Private L., 8,148, was wounded by shrapnel on March 11, 1915. He was completely blind for two days and had had much headache. There were several shrapnel wounds in the scalp, but the bone was injured only under a triangular wound immediately to the left of the inion. An X-ray examination showed a comminuted fracture in this region with depressed

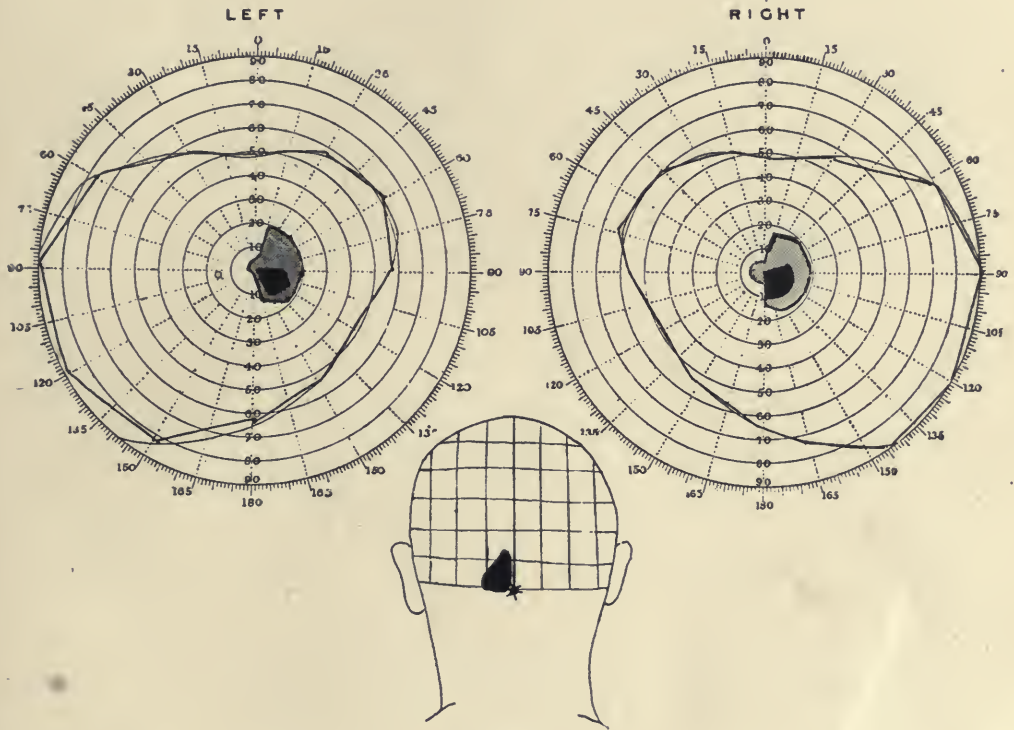


FIG. 11.

fragments of bone in the brain beneath it, and a linear fracture running upwards and outwards to the left parietal eminence. When first seen, four days after the injury, he had complete right hemianopia and some defect of central vision. When his fields were taken eight days later, the peripheral fields were full, but a right absolute paracentral scotoma was discovered which extended outwards to about 20° and inwards to the fixation point. This was surrounded by a partial scotoma which invaded the left halves of the fields to the extent of about 10° round the fixation point. At this time he was unable to read even large letters. Both the complete and the partial scotomata gradually decreased in size, and about three weeks after the infliction of the wound there was only

a small absolute paracentral scotoma in the right lower quadrant, which was surrounded by an area of defective vision. The latter extended to about 5° to the left of the fixation point (fig. 11). At this time he was able to read only the largest letters.

In this case the main injury must have been at the tip of the left occipital pole, but the right occipital pole was probably also damaged to a slight extent.

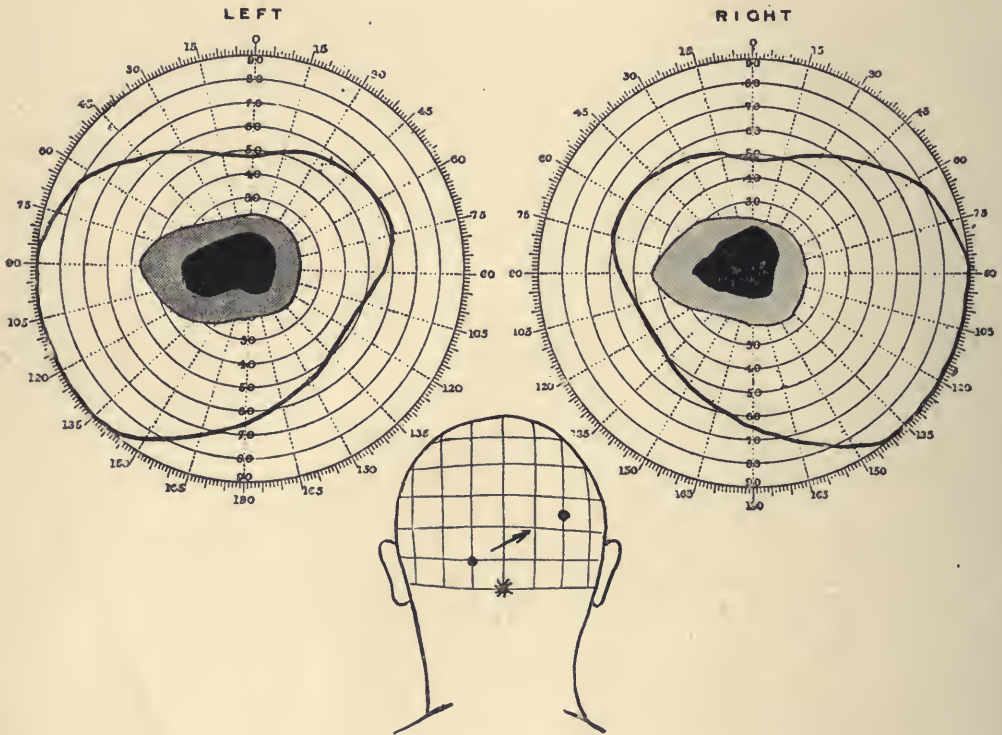


FIG. 12.

Case 9.—Lieutenant T. was wounded on December 20, 1914, by a bullet. He was unconscious for a time, and on coming round found he was quite blind, and had a sensation of positive blackness in front of his eyes. He first noticed, about four days later, the white aprons of the sisters passing by his bed.

Wound.—The entrance lay about 1 in. (2.5 cm.) above the level of theinion and 1 in. (2.5 cm.) to the left. The exit was $2\frac{1}{2}$ in. (6.25 cm.) above theinion and 2 in. (5 cm.) to the right of the middle line. An X-ray plate showed a depressed fracture of the skull and fragments lying in and on the brain. He was operated on by Mr. Hugh Lett on December 23. A

large horseshoe flap, which included the two wounds, was turned down. Brain matter at once escaped from the entrance. The openings in the bone on both sides were enlarged and the intervening bridge of skull removed. The dura had been torn from one opening to the other, and the damaged brain bulged through it after irregular fragments had been removed from both occipital lobes. The patient made an uninterrupted recovery. The visual fields were taken eleven days after injury; there was then a large absolute central scotoma extending about 10° on the right of the fixation point and to nearly 20° on its left. This was surrounded by a zone of partial vision (fig. 12). From this time his sight improved considerably till he was discharged twenty-six days after the injury. There was then very imperfect central vision, with an absolute paracentral scotoma below the fixation point, which was surrounded by an area of incomplete vision. He was now able to recognize large letters. The peripheral limits of the visual fields were unrestricted.

In this case the course of the missile and observation of the injury at the time of operation make it certain that the tip of each occipital lobe was seriously damaged.

HOMONYMOUS HEMIANOPIA WITH CENTRAL SCOTOMA.

Another interesting group of cases that we have observed has been distinguished by the presence of homonymous hemianopia with a central scotoma. In all these the missile, which had an oblique course, caused extensive injury of the occipital lobe or optic radiations of one side, and passed through or near to the tip of the occipital pole of the opposite hemisphere.

Case 10.—Private G., 10,634, was probably injured on March 26, 1915, by a rifle bullet. He was completely blind for two or three days, and then began to distinguish light to the left side. He was admitted to a base hospital five days later. He had been operated upon in the casualty clearing station on the day following the injury. He was at first very drowsy and had some difficulty in understanding speech, but this rapidly cleared up.

Wound.—The entrance was 2 in. (5 cm.) above and $1\frac{1}{2}$ in. (3.75 cm.) to the right of the inion. The exit was represented by a large circular defect in the scalp about $1\frac{1}{2}$ in. (3.75 cm.) to 2 in. (5 cm.) in diameter, through which softened and disintegrated brain protruded. Its centre was $2\frac{1}{2}$ in. (6.25 cm.) above and $1\frac{1}{2}$ in. (3.75 cm.) to the left of the inion. An X-ray photograph showed a large bone defect under the exit wound, which reached to the middle line and extended almost down to the inion. There was no paralysis or sensory disturbance, and his reflexes were normal. At first he had vision only in the left upper quadrants, but later vision returned in the whole periphery of the left visual field, but a large central scotoma extending to about

20° to the left of the fixation point persisted till he was transferred to England, a month after the infliction of the wound (fig. 13).

In this case there can be no doubt that the posterior part of the optic radiations of the left hemisphere, and probably a considerable part of the calcarine cortex, were destroyed by the missile and by the secondary changes involved in the hernia formation, while on the right side the bullet merely passed through the posterior extremity of the occipital lobe.

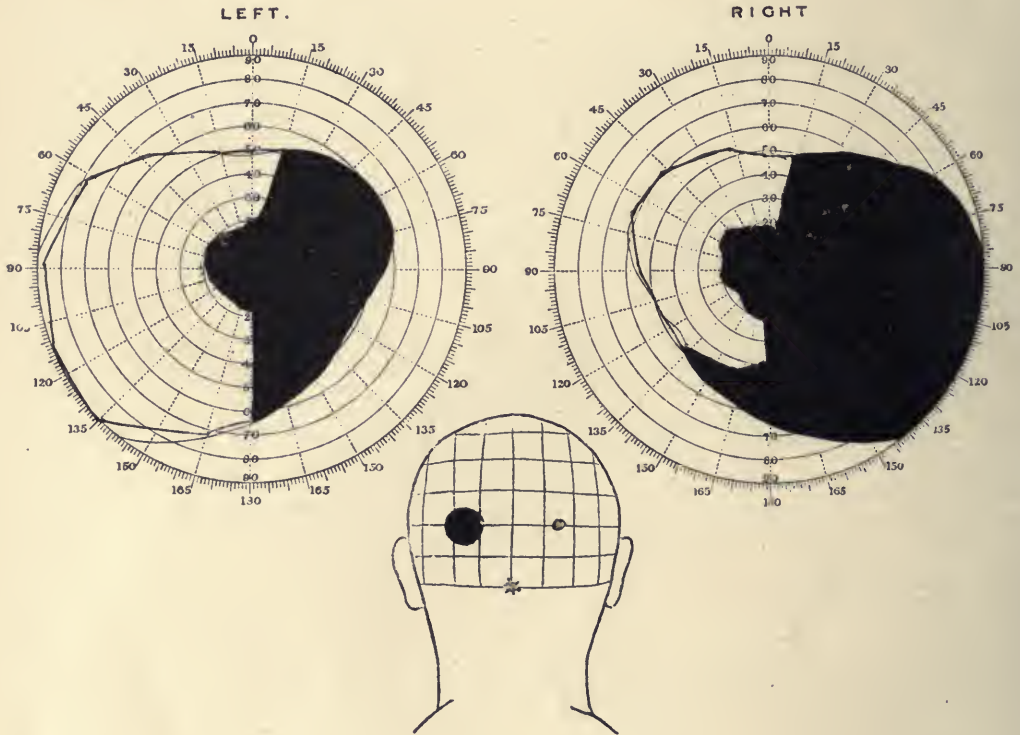


FIG. 13.

Case 11.—Private M., 1,424, was wounded by a rifle bullet on September 25, 1915. He was blind for the first two days, and had a sensation of blackness in front of his eyes. He reached the base three days later, and then presented no abnormal symptoms apart from visual disturbance.

Wound.—The entrance was 2 in. (5 cm.) above and 3 in. (7.5 cm.) to the left of the inion. The exit was 2 in. (5 cm.) to the right and 2 in. (5 cm.) above the inion. An X-ray photograph showed under the entrance wound a defect in the skull at the lambdoid suture, with many fragments of bone driven into the brain, while the exit was represented by a blown-out wound to the right of and slightly above the inion. The visual fields, taken three weeks after

injury, showed complete right-sided homonymous hemianopia and a central scotoma which extended to just beyond 10° to the left of the fixation point (fig. 14). His vision remained in this state till he was transferred to England.

In this patient the injuries were similar to those in Case 10. The left optic radiations must have been injured by the depressed fragments of bone and by softening under the wound of entry, while owing to the oblique course of the missile it is probable that only the posterior extremity of the hemisphere was damaged on the right side, and chiefly on its mesial surface.

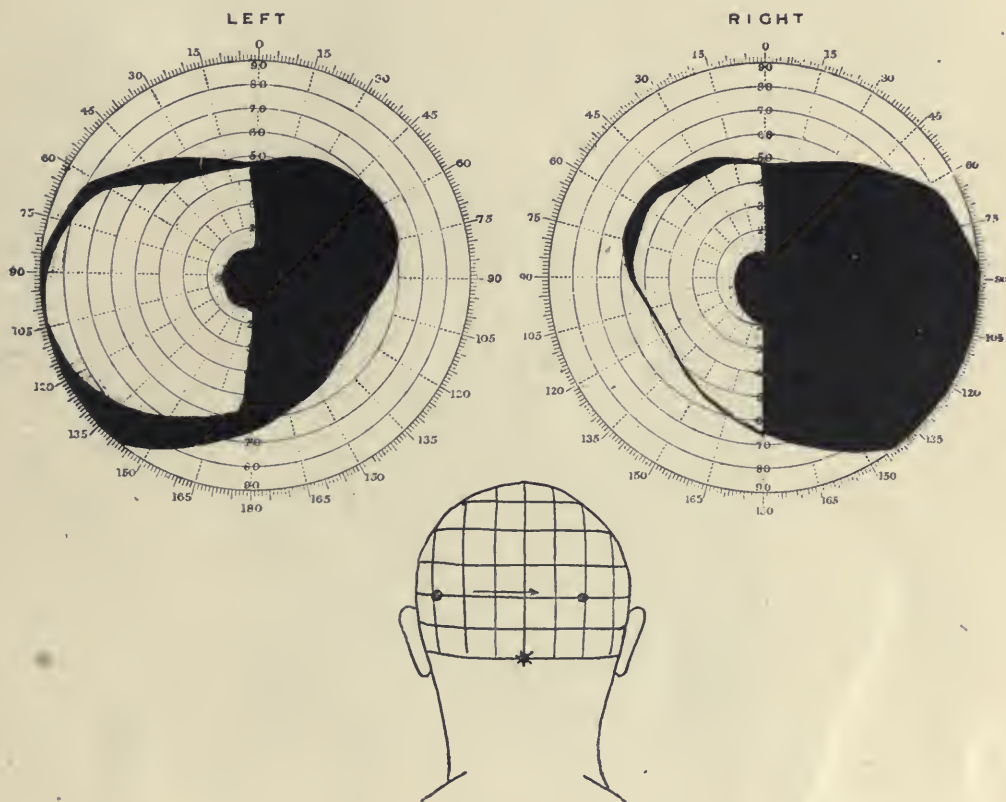


FIG. 11.

Case 12.—Private M., 16,694, was admitted to a base hospital on January 13, 1916. He was then quite blind, but a few days later could recognize light in the left periphery of his visual fields.

Wound.—The entrance was $1\frac{1}{2}$ in. (3.75 cm.) above and $3\frac{1}{2}$ in. (9 cm.) to left of theinion; exit $1\frac{1}{2}$ in. (3.75 cm.) above and $1\frac{1}{2}$ in. (3.75 cm.) to right of theinion. An X-ray photograph showed fragments of bone driven into the brain beneath the entrance wound. There was no paralysis, sensory or speech

disturbances, or alteration in his reflexes. The depressed fragments of bone with some disintegrated brain were later removed from the wound of entrance, but owing to the spread of infection to the ventricle and the occurrence of meningitis, he died five weeks after the infliction of the wound. The visual loss was so extensive that it was never possible to take his visual field with a perimeter, but during the whole time he was under observation he had complete right homonymous hemianopia with an absolute central scotoma, which extended for about 20° to 30° to the left of the fixation point. At the autopsy a large septic wound was found in the left occipital lobe, which involved all the structures lateral to the ventricle, including the optic radiations. On the right side the bullet had, in passing, destroyed about the posterior third of the calcarine cortex (fig. 15). The brain was not infected on this side, and the rest of the area striata was undamaged.



FIG. 15.—Photograph of mesial surface of the right occipital lobe in Case 12, showing superficial damage at the posterior extremity of the calcarine fissure.

In these seven cases (Cases 6 to 12), there were absolute central scotomata of various sizes. In the first four peripheral vision was unaffected, but in Cases 10, 11, and 12 the central scotomata were associated with homonymous hemianopia.

In those cases in which there was a pure central scotoma the lesion was, as far as it is possible to judge from the course of the missile, from the evidence afforded by radiographic examination, and from the conditions found at operation, limited to the posterior ends of the occipital

lobes at or about the level of the posterior extremities of the calcarine fissures. Consequently it is probable that only the hindermost ends of the *area striata* were damaged. This was obviously so in Cases 7 and 9, while in Case 6 the depression of the inner table must have bruised and probably produced softening of the occipital poles. In Case 8 the cranial injury, it is true, was unilateral, but it is the common experience that such depressed fractures due to shrapnel or fragments of shell-casing often produce relatively diffuse damage; further, in this case the visual symptoms diminished rapidly, so that when he was last examined the absolute scotoma was only paracentral; its position in the right halves of the visual fields corresponded with complete functional abeyance of a portion of the left *area striata*, and it was over the posterior part of this that the lesion actually lay.

These observations, associated with the fact that among over 2,000 cases of head injury we have never seen a central scotoma when a direct injury of the occipital poles could be excluded, afford strong evidence that central vision is represented on either the mesial or the lateral surface of the poles of the occipital lobes. Further, our observations conform to the generally accepted view that the visual area corresponds with, or at least includes, the *area striata*.

Those cases (10, 11, and 12) in which there was a homonymous hemianopia in addition to a central scotoma also conform to or support this view. In Cases 10 and 11 the hemianopia was probably due to the extensive lesions on the lateral surfaces of the occipital lobes on one side, which involved the optic radiations, while, owing to its oblique course, the missile can have injured directly only the posterior pole of the opposite hemisphere. In Case 12, in fact, in which the visual fields were, as far as could be ascertained by rough methods of examination, very similar to those of the two preceding cases, the optic radiations and the greater part of the calcarine cortex were destroyed on the left side, while in the right hemisphere the destruction involved only the posterior part of the *area striata*; and this lesion corresponded with loss of central, but with intact peripheral vision in the left halves of the visual fields.

It is true that in all such lesions afferent sensory tracts must be damaged in addition to the cortex, but as the fibres of the optic radiations destined for the anterior extremity of the *area striata* do not extend farther posteriorly than the horn of the ventricle (fig. 3), it can be assumed that when the lesion is limited to the occipital pole centripetal fibres to this region only are involved.

The evidence so far consequently points to representation of the macula at the posterior pole of the hemisphere. This conclusion is strongly supported by the next group of visual disturbances with which we shall deal.

PARACENTRAL SCOTOMATA.

We have seen a considerable number of cases with paracentral scotomata—that is, isolated areas of blindness in the visual fields which lie to one side of the fixation point, but do not involve it.

Case 13.—Private B., 416,152, was wounded by a round shrapnel bullet. He was unconscious for some time, and his state on admission made it impossible to obtain an accurate history.

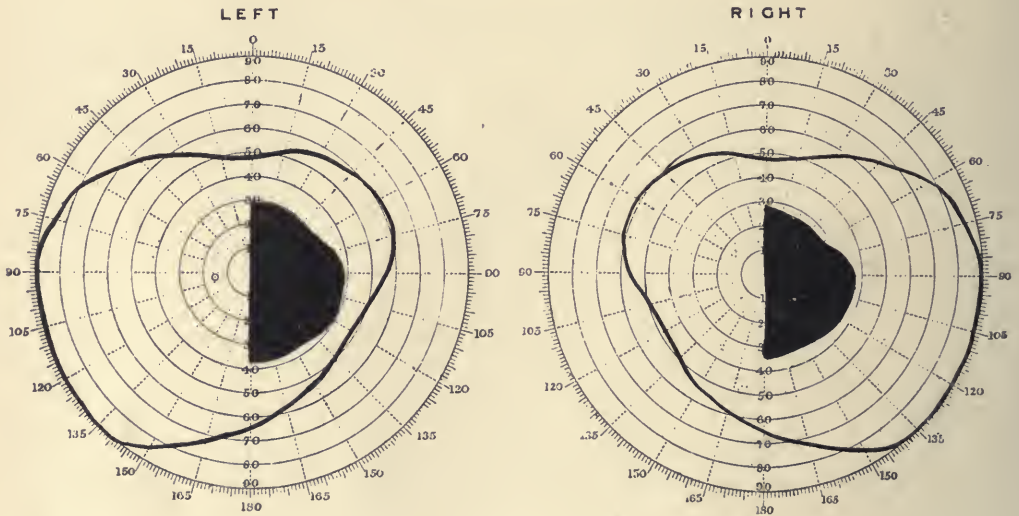


FIG. 16.

Wound.—The entrance was immediately below theinion in the middle line, and an X-ray photograph showed the bullet immediately inside the skull at the base of the left mastoid process. It was removed from this position the next day. An extensive injury of the left lateral lobe of the cerebellum was discovered. The occipital lobes were not examined, but the bone was widely fractured over the pole of the left hemisphere. Recovery was uninterrupted. When he was first examined, he had probably a right hemianopia, but his state did not permit a thorough examination. Four weeks later, however, when he was able to sit up, only a paracentral scotoma to the right of the fixation point was discovered. It extended from the fixation point, both above and below the horizontal level, and outwards to about 30° (fig. 16).

In this case the exact extent of the injury of the visual area was not determined, but probably its posterior part was most seriously damaged.

Case 14.—Private B., 13,426, was wounded by a piece of shell-casing on February 3, 1916. For an hour or so he had a "dim mist" in front of his

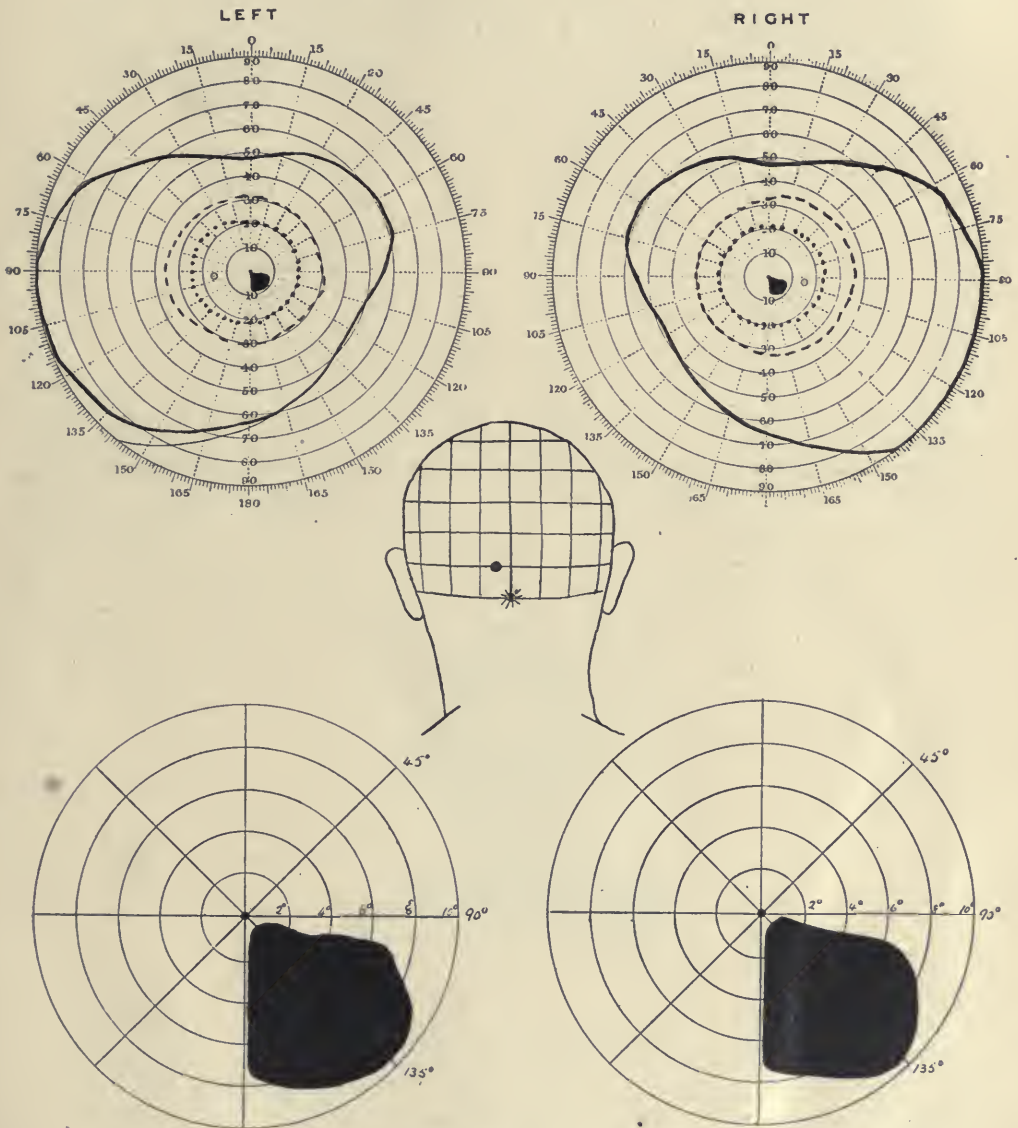


FIG. 17.

eyes, but this gradually disappeared, and when he was admitted to the base hospital two days later he was unaware of any defect in sight.

Wound.—A small contused scalp wound, the centre of which was 1 in.

(2.5 cm.) above and $\frac{1}{2}$ in. (1.25 cm.) to the left of theinion. An X-ray photograph showed a narrow crack in the outer table and a small depression of the inner table immediately under the wound. The scalp wound was excised, but the skull was left untouched. When the visual fields were taken, twelve days after the infliction of the wound, the limits to those for white, red, and green were unrestricted, but there was a small absolute scotoma in the right inferior quadrant which reached to within 1° of the fixation point, and extended outwards

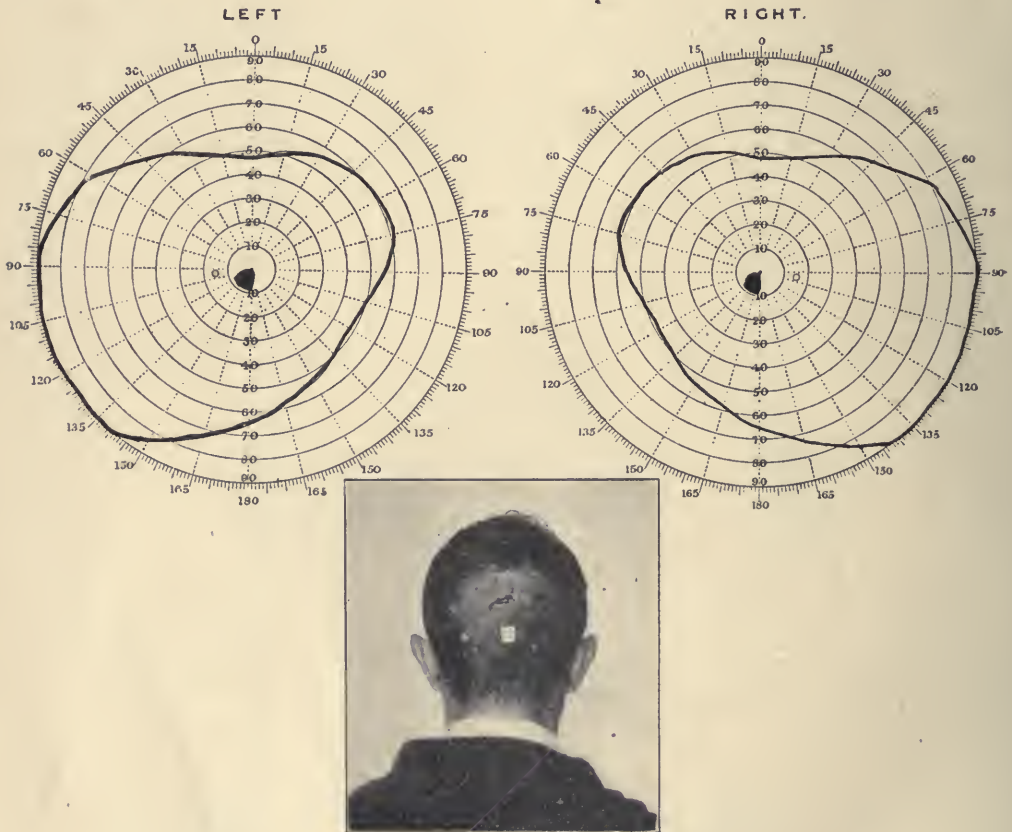


FIG. 18.

to 10° (fig. 17). The areas over which perception of white and that of colours were lost were identical.

The position of the wound and the X-ray examination make it probable that in this case there was a contusion of the left occipital pole at the upper lip of the calcarine fissure.

Case 15.—Lieutenant H. was wounded on November 5, 1915, by a bullet. He noticed at first he could not see his feet, [but his vision improved rapidly,

and when he was first seen by us four days later, his only complaint was that on attempting to read he could not see the four or five lines immediately below that which he was reading, though the rest of the page was visible to him.

Wound.—A tangential scalp wound with its entrance 1 in. (2.5 cm.) above and $1\frac{1}{2}$ in. (3.75 cm.) to the right of the inion, while the exit was in the middle line and $\frac{1}{2}$ in. (1.25 cm.) above the inion. An X-ray photograph showed no definite changes in the skull. Examination of visual fields revealed a small absolute paracentral scotoma for white and colours which lay chiefly in the left lower quadrants; it extended up to the fixation point and downwards and outwards to about 9° (fig. 18). This condition remained unaltered three weeks after the infliction of the wound.

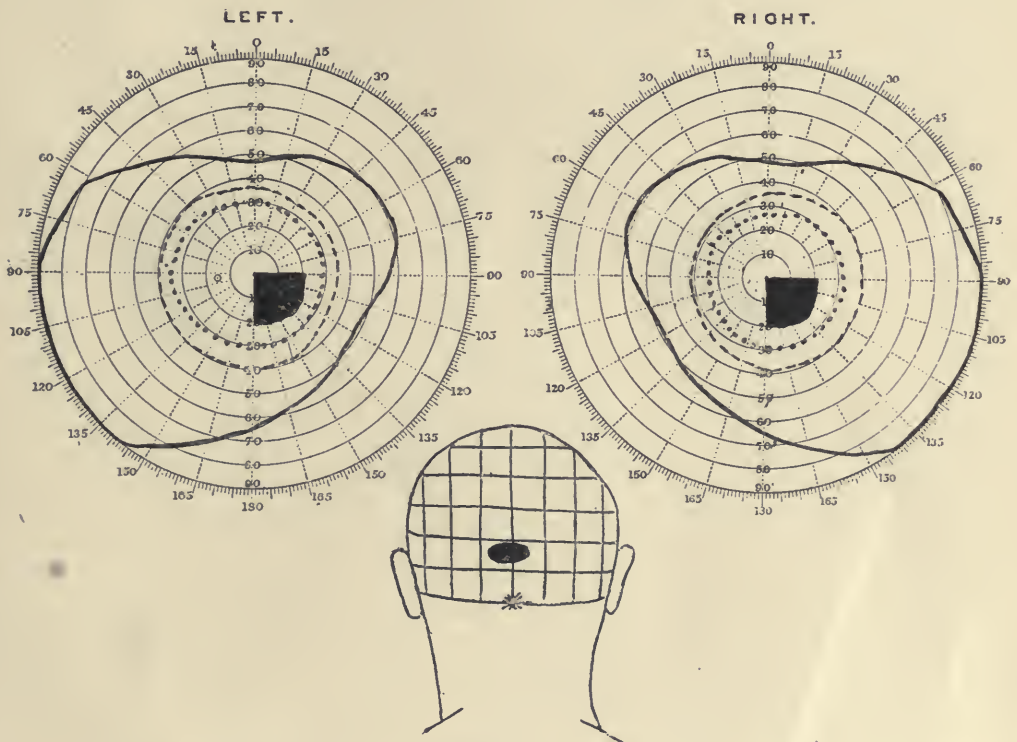


FIG. 19.

In this case the wound lay immediately above the posterior extremity of the upper lip of the right calcarine fissure.

Case 16.—Private A., 17,385, was wounded on February 12, 1916, by a piece of shrapnel. He did not become unconscious, but noticed his sight affected immediately. He was operated upon at a casualty clearing station on the following day, when a depressed fracture of the occipital bone was found over the longitudinal sinus. The dura was probably undamaged. When

admitted to the base five days later there was a transverse wound across the middle line $1\frac{3}{4}$ in. (4.5 cm.) above the level of the inion, and an X-ray photograph revealed a defect in the skull midway between the inion and lambda in the middle line. Perimetric examination showed that the peripheral limits of white and colours were unrestricted, but there was an absolute scotoma for both white and colours in the right lower quadrants which extended from the fixation point to about 20° outwards and downwards (fig. 19). His central vision was $\frac{6}{9}$ in each eye.

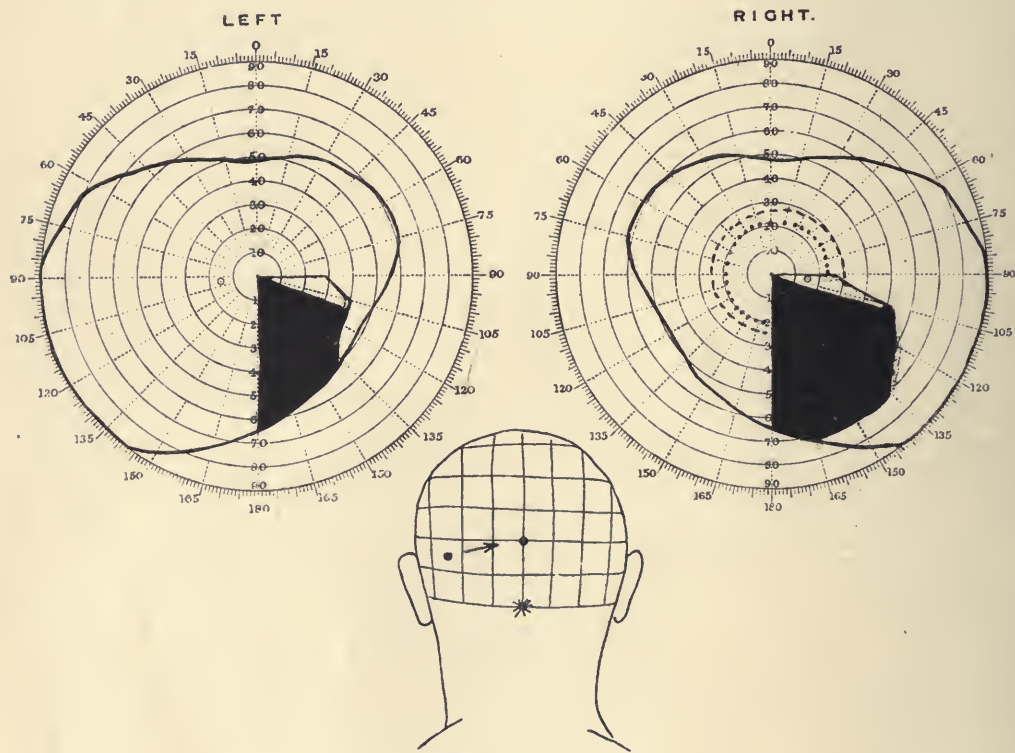


FIG. 20.

Case 17.—Lieutenant F. was wounded March 13, 1915, by a bullet. His sight at once became indistinct. Two days later he was operated upon at a casualty clearing station.

Wound.—Entrance was $1\frac{1}{2}$ in. (3.75 cm.) above and $2\frac{1}{2}$ in. (6.25 cm.) to the left of the inion. The exit was in the middle line and 2 in. (5 cm.) above the inion, and they were joined by a healed incision, beneath which a defect in the skull could be felt. Perimetric examination was first made a fortnight later. He then had a complete scotoma for white and colours in the right inferior quadrants which reached from the fixation point to the limit of the

normal field immediately below; but to the right of this there was peripheral vision to both white and large areas of colour, which shows that the defect in the field was of the nature of a paracentral scotoma rather than a quadrantic loss (fig. 20). At the upper border of the scotoma the blindness was only partial from the horizontal line to 15° below it.

In this case the extent of the damage was uncertain, but the wound lay over the upper and posterior portion of the left area striata.

Case 18.—Sergeant D., 16,197, was wounded by a fragment of a high-explosive shell on March 2, 1916. He was dazed for a moment, but not unconscious, and noticed at once "stars and very brilliant revolving things" in front of his eyes, whether they were open or closed; when he arrived at

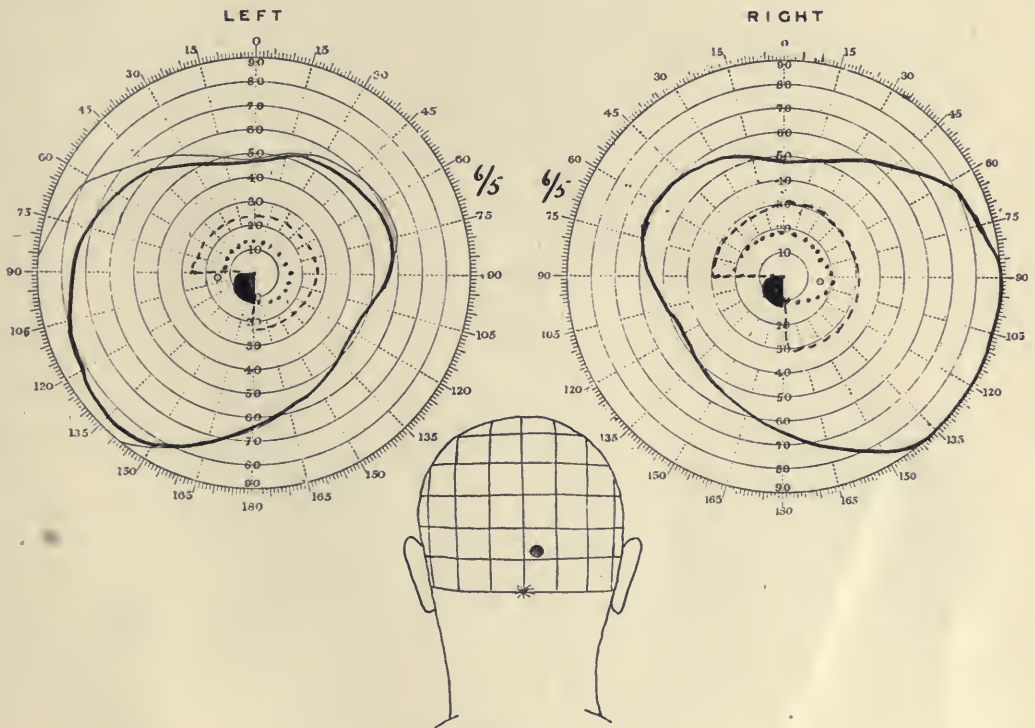


FIG. 21.

the base, he was unable to say if these visual spectra had appeared more to one side than to the other. It seemed to him, too, that there was a mist in front of his eyes, but his vision improved rapidly.

The wound was a small gaping incision $1\frac{1}{2}$ in. (slightly more than 3 cm.) above the inion, and slightly to the right of the middle line. This was explored next day, and a small depressed fracture, in which a piece of metal was

impacted, was found immediately to the right of the longitudinal sinus and $1\frac{1}{4}$ in. (slightly more than 3 cm.) above the apex of the inion.

His visual fields were first taken three days after the infliction of the wound, and again three weeks later. On each occasion a small paracentral absolute scotoma, which extended up to the fixation point, was found in the left lower quadrants; vision for red and green was lost beyond this, and vision for white objects 5 mm. square was indistinct. Otherwise there was no peripheral restriction of vision for white or colours (fig. 21). His central vision after correction was $\frac{5}{8}$ in each eye.

The exact position of the depressed fracture was carefully measured in this case at the time of operation, and its position was found to correspond with the posterior extremity of the upper lip of the calcarine fissure.

Case 19.—Private C., 12,993, was wounded by a rifle bullet on January 5, 1916. He was unconscious for two hours, and then found his sight much affected; it rapidly improved, however.

Wound.—The entrance was 2 in. (5 cm.) to the left, $\frac{1}{2}$ in. (1.25 cm.) above the inion; exit 1 in. (2.5 cm.) to the right and slightly lower than the inion. An X-ray examination showed a medium-sized entry wound in the skull with depressed bone beneath it, and an exit with out-driven bone immediately to the right of the inion. Two days after arrival at the base he was operated upon. A horse-shoe flap was turned down, and it was seen that the entrance lay just above the lateral sinus on the left side. This was firmly thrombosed. A large flake of bone was removed from the brain and several small pieces, as well as a firm clot from the upper margin of the cerebellum. He made a rapid recovery. His visual fields were first examined three weeks after infliction of the wound. There was an absolute paracentral scotoma in the right upper quadrants which extended from the fixation point outwards to 20° , and projected slightly below the horizontal. This was surrounded by an area of partial scotoma, in which white was dull and indistinct, and colours not recognized with certainty. The peripheral limits of the fields for white and red were unrestricted, but green objects of 10 mm. square could not be recognized to the right of the scotoma. The absolute scotoma, when measured by Bjerrum's screen, was found to extend up to less than 1° of the fixation point (fig. 22). His visual acuity was, however, $\frac{6}{9}$. The only complaint of vision he made was that in reading he had occasionally lost his place. His visual fields were repeatedly taken, but remained unaltered till he left for England six weeks after the infliction of the wound.

There can be no doubt that in this case the occipital pole was injured chiefly below the extremity of the left calcarine fissure.

Case 20.—Private T., 868, was wounded on March 6, 1916, by a fragment of shell. He was unconscious for a short time, but apart from some headache he was not aware of any abnormal symptoms. He arrived at the base two days later.

Wound.—There was an irregular gaping wound about $\frac{1}{2}$ in. (1.25 cm.) above

the apex of the inion and immediately to the left of the middle line. The bone was exposed and was seen to be fractured and depressed. An X-ray examination showed that the skull was comminuted and depressed immediately

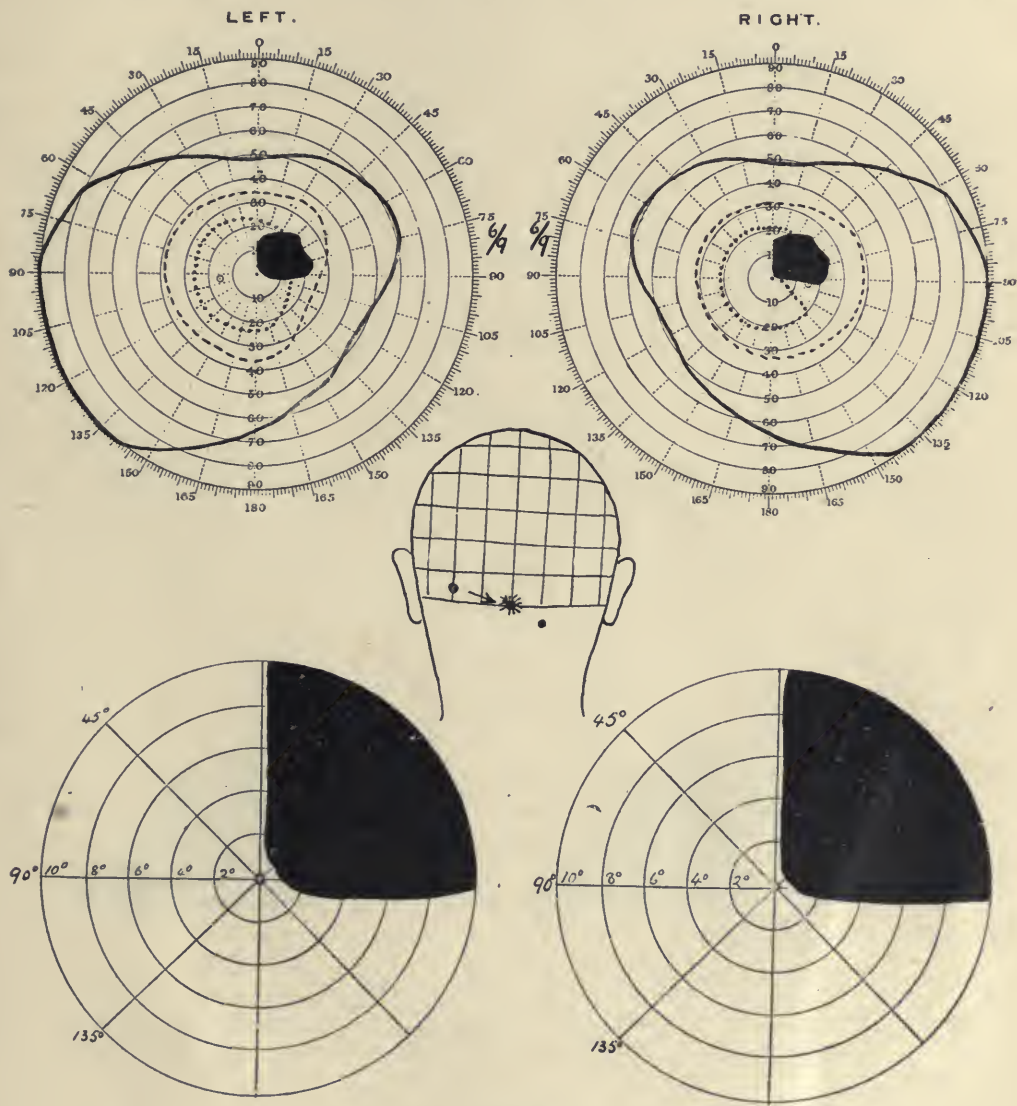


FIG. 22.

above the level of the internal occipital protuberance. When first seen his vision was $\frac{6}{12}$ in each eye, and he was unaware of any disturbance of vision, but examination revealed a small paracentral scotoma in the right upper quadrant, which extended to the fixation point.

A few days after admission to hospital, a flap was turned down over the occipital pole, and then a crater-like depression was seen in the skull, the centre of which was immediately to the left of the middle line and about $\frac{1}{3}$ in.

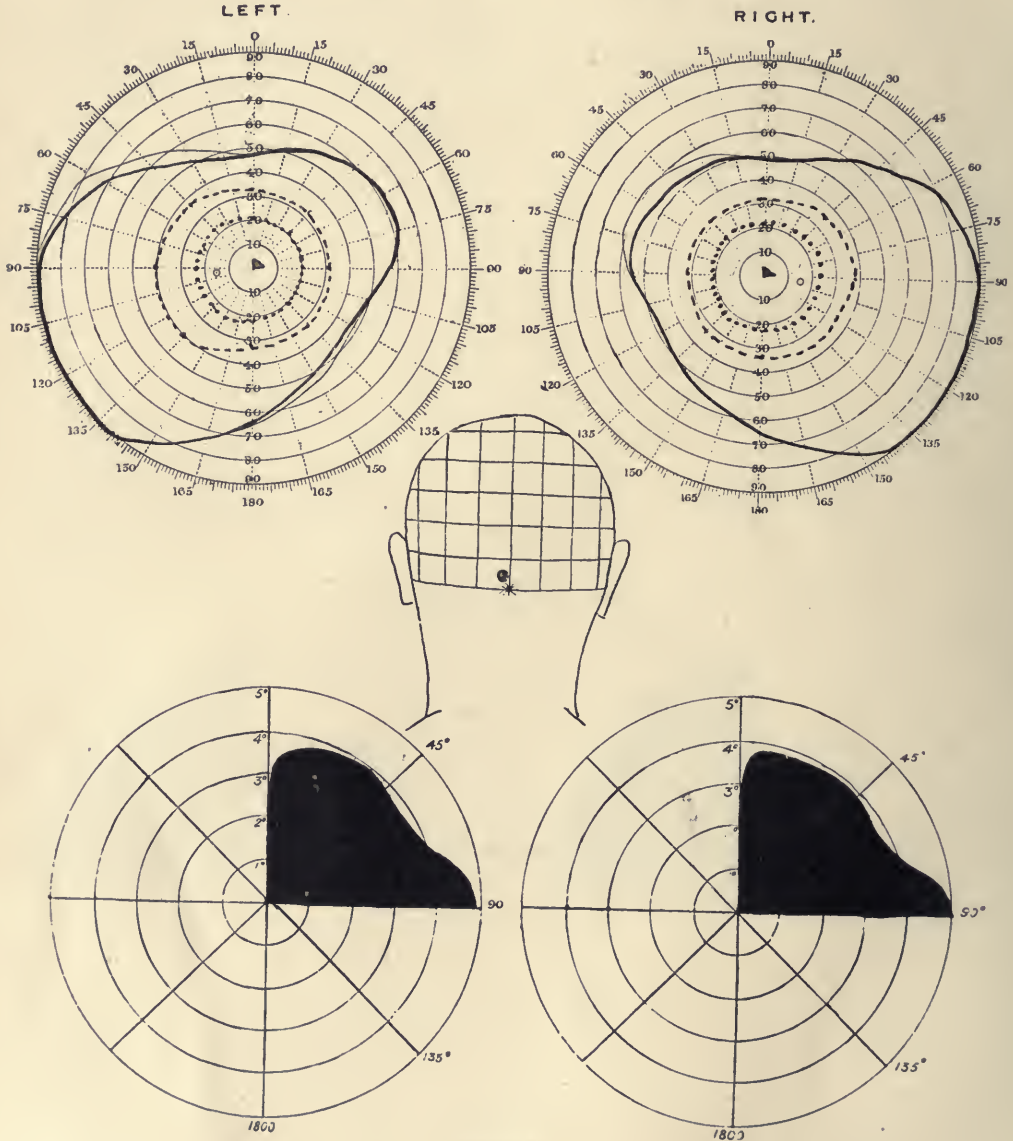


FIG. 23.

(about 0.75 cm.) above the inion. In order to remove the depressed bone, a trephine opening was made to the left of it, and it was there found that a large area of the inner table which had been driven in had lacerated the left lateral

sinus and bruised the inferior surface and the tip of the left occipital pole. The wound healed rapidly. He remained under observation till five weeks after the infliction of the injury.

His visual fields were repeatedly examined, but remained practically unchanged. The peripheral limits of the fields for white, red and green (objects 5 mm. square) were normal, but, as above mentioned, there was a small paracentral scotoma in the right superior quadrant which extended from the fixation point to about 5° outwards. The perception of colours was lost over the same area (fig. 23). He was not aware of this defect and could read quite well. His central vision five weeks after the infliction of the wound was $\frac{6}{9}$ in each eye.

In this case it was definitely determined at the operation that the left occipital lobe was injured at the posterior and inferior aspect of its pole.

Case 21.—Lance-Corporal G., 2,541, was wounded by a bullet as he was bending forward on January 26, 1916. He was unconscious for half an hour or so, and afterwards noted his sight was slightly affected.

Wound.—There was a long oblique wound which extended from the middle line of his skull about 2 in. (5 cm.) above inion, downwards and to the left for a distance of $2\frac{1}{2}$ in. (6.25 cm.). On separating the edges of the wound a narrow gutter defect was found in the skull through which disorganized brain protruded. An X-ray examination showed a large flake of bone driven into the left occipital pole. Three days after the injury the depressed bone was removed and some softened brain washed away. His head wound healed rapidly. The bullet had also passed through the posterior part of his left shoulder. His fields were first carefully examined by the perimeter one month after the injury. There was found a large paracentral scotoma, which extended from the fixation point into the right halves of the fields to the extent of 20° to 30° , and in the lower portion of the left halves of the fields to the extent of 25° (fig. 24). The peripheral limits of vision for white were normal, but green and red objects 10 mm. in diameter were visible only to the left of the vertical line. Examination by Bjerrum's screen showed that the blindness extended to less than $\frac{1}{4}^{\circ}$ from the fixation point. His visual acuity was $\frac{6}{8}$ in each eye. His fields were taken repeatedly, but remained practically unaltered till he left for England six weeks after his injury was inflicted.

In this case the left occipital pole, both above and below the level of the calcarine fissure, must have been extensively damaged, while the right hemisphere was probably injured at the level of the upper part of the wound by the in-driven flake of bone, which had probably penetrated the falx cerebri. The exact extent of the lesion could not be accurately determined at operation.

In these nine cases the paracentral scotomata, of various sizes appeared on ordinary perimetric examination to reach immediately to the fixation point, and on more careful investigation by a Bjerrum's screen they were found to come within at least 1° of it. If the fovea centralis subtends an angle of 4° to 6° (Starling), vision subserved

by it would be consequently involved. In these cases the lesions were in all probability relatively superficial, except in Case 17, and in all

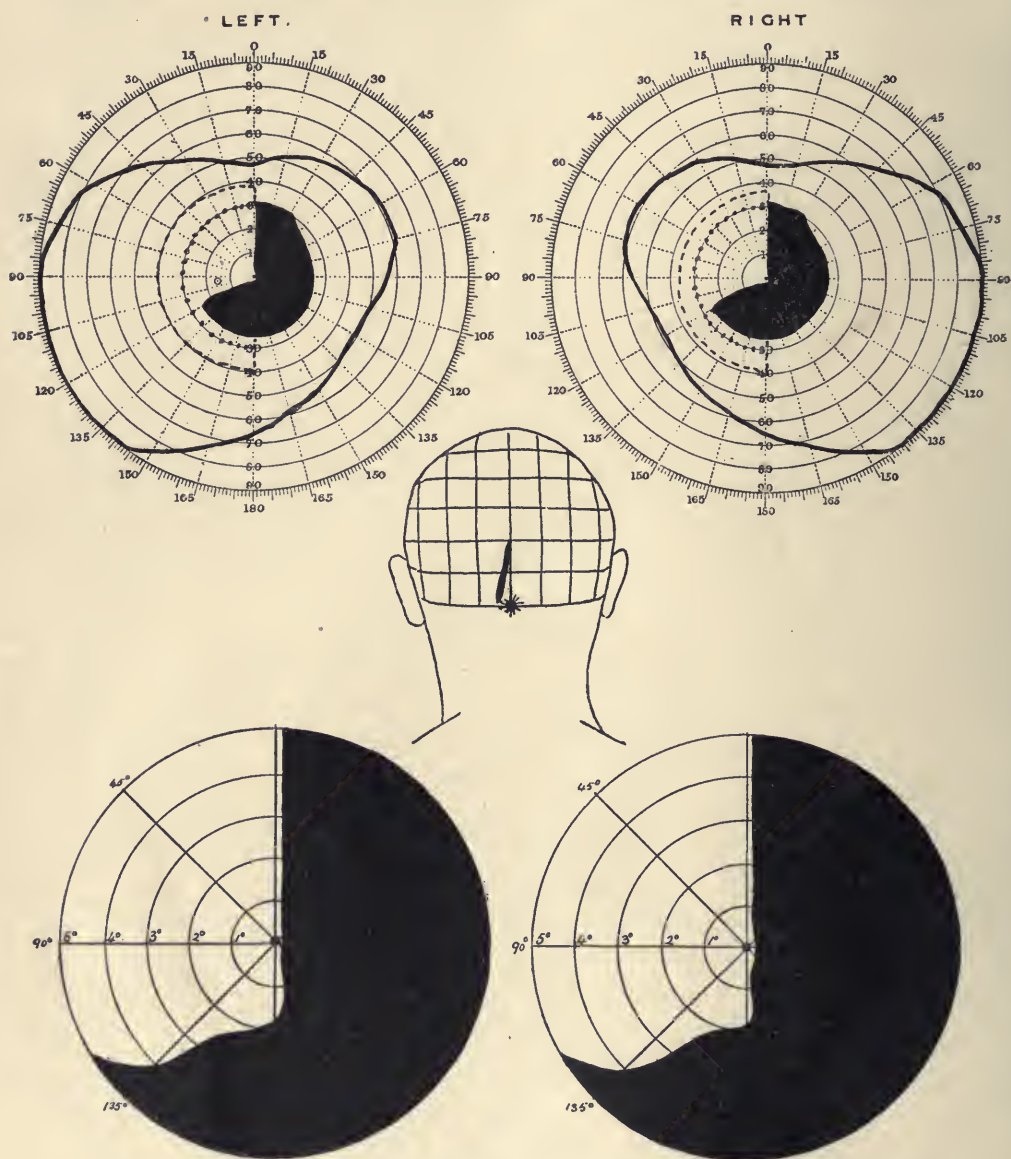


FIG. 24.

they lay over or in the neighbourhood of the posterior extremity of the one calcarine fissure. They consequently support the conclusion already

put forward that central vision is represented in the posterior parts of the occipital lobes. Further, it will be observed that in Cases 14 to 18, in which the paracentral scotomata were limited to the lower quadrants of the visual fields, the main lesions probably lay above the level of the posterior extremity of the calcarine fissures; this fact consequently confirms the conclusion that the upper half of each retina is represented in the dorsal part of the area striata. Cases 19 and 20 are the only two we have yet seen with superior paracentral scotomata; in these the brain was damaged on the under surface of the pole, and it is consequently evidence that those portions of the lower quadrants of the retina in the neighbourhood of the fovea are represented in the lower and posterior parts of the *area striata*.

In Case 21, in which we found a triquadrantic scotoma, the whole breadth of the posterior part of the visual cortex was probably destroyed on the left side. The defect in the left visual field, which, it will be noticed, did not reach the fixation point, was probably due to an injury of the mesial surface of the right hemisphere.

We can consequently conclude that not only is central vision represented towards the posterior part of the occipital lobe, but also that the upper portion of the retina in the immediate neighbourhood of the macula corresponds with the upper and most posterior part of the *area striata*, while the central portion of the retina below the level of the macula is represented in its lower and posterior part.

It is obviously impossible to draw definite conclusions from material such as ours, since our clinical observations have not been controlled by anatomical examinations, but we can suggest tentatively that the portion of the *area striata* which extends to the margin and on to the lateral surface of the occipital lobe is the cortical focus of central vision. For in the first place, in all the scotomata we have observed associated with injury to this region the blindness involved, or reached to within 1° of the fixation point, though their sizes varied considerably; in other words, the fixation point or its immediate vicinity was that portion of the visual field which was constantly affected by posterior occipital lesions.

In the second place, in such cases as 6, 14, 15 and 18 the depression of bone upon, or the effects of concussion immediately over, the posterior aspect and the lateral surface of the occipital lobe produced a local disturbance of vision which extended up to or involved the fixation point.

Again, if the macula is represented on the posterior aspect of the

hemisphere we should expect that wounds which penetrate the occipital lobe at the level of the extremity of the calcarine fissure would produce homonymous blindness reaching to the fixation point, and this we have actually found to be the rule. The following case illustrates it:—

Case 22.—Lieutenant C. was wounded by a bullet May 9, 1915. He was unconscious for some time and could give no history. When admitted to the base hospital three days later he was very dull and could recognize objects only to the right of the fixation point.

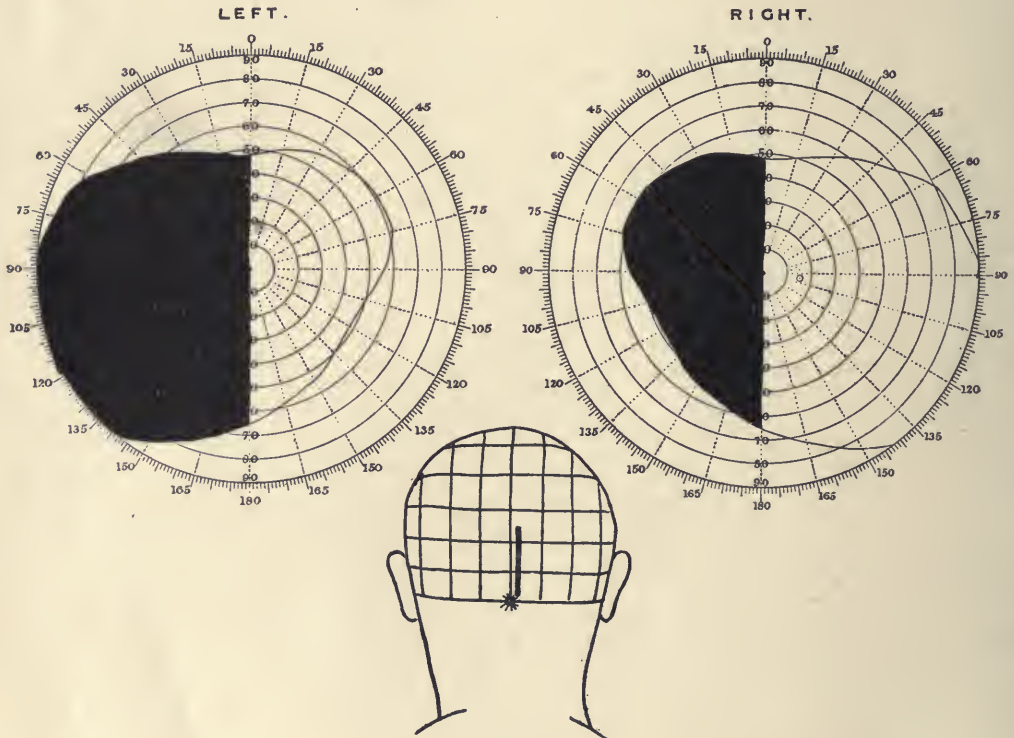
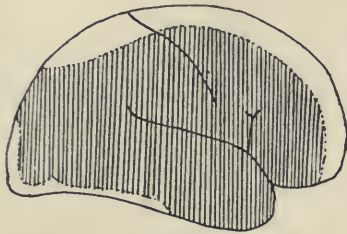


FIG. 25.

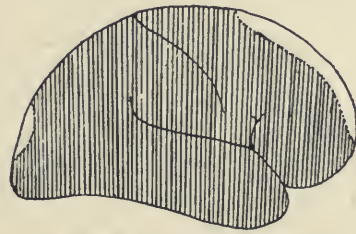
Wound.—There was a gaping gutter wound on the right side, parallel and close to the middle line, which extended from the inion $2\frac{1}{2}$ in. (6.25 cm.) upwards. X-ray examination showed a linear defect in the skull and several pieces of bone driven deeply into the brain. An operation was performed the next day; a hole in the skull 2 in. by $\frac{1}{2}$ in. (5 cm. by 1.25 cm.) was found; the dura was lacerated for 1 in. above the inion and immediately to the right of the longitudinal sinus. Disintegrated brain protruded through it. Fragments of bone were removed from a long track, which passed directly forwards to a

depth of about 2 in. (5 cm.). There was considerable destruction of brain around the track. A perimetric examination was made two weeks after infliction of the wound; he had then complete left hemianopia extending right up to the fixation point (fig. 25).

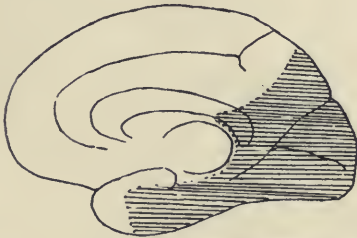
But any such hypothesis on the cortical localization of central vision must be capable of explaining all generally accepted facts. The most important of these is the frequent escape of macular vision in homonymous hemianopia due to vascular occlusion. The explanation probably depends on the vascular distribution in the region of the occipital



Area of most common distribution
of the middle cerebral.



Area of maximal distribution
of the middle cerebral



Area of most common distribution of the posterior cerebral.



(from Beevor)

FIG. 26.

pole. According to Beevor's classical work on the distribution of the cerebral vessels, the occipital pole is usually supplied by the posterior cerebral artery, but the middle cerebral extends usually to within $\frac{1}{2}$ in. to $\frac{1}{4}$ in. (1.25 cm. to 0.7 cm.) of it, and occasionally actually includes it (fig. 26). The occipital pole, and particularly its lateral aspect, is consequently a watershed area between these two large vessels; it may under normal conditions draw blood from both, and if one is blocked the other may suffice to maintain its nutrition. It is, in fact, well known that the softening due to occlusion of any cortical artery is rarely as extensive as its anatomical distribution. If this view is correct the presence or

absence of macular escape in hemianopia due to vascular lesions may be explained by the varying degree of anastomosis between, and the relative extent in the distribution of, the posterior and the middle cerebral arteries at the occipital pole of the hemisphere. The frequent persistence of central vision in bilateral hemianopia due to bilateral cortical lesions may be possibly explained by this same fact.

To make our conclusions complete it would be necessary to bring forward evidence on the cortical representation of peripheral vision. If the macular centre lies in the posterior part of the area striata, and if, as we find, lesions here do not affect peripheral vision, it might be assumed that the latter is represented in the more anterior part of the visual zone; and the fact that the size of the scotoma, whether central or paracentral, varies directly with the depth of the wound from the occipital pole, makes it probable that the concentric zones of the retina from its centre outwards are represented in serial order from behind forwards in the visual area.

We have not had, however, the opportunity of observing any positive case that bears conclusively on the cortical localization of peripheral vision. This is not surprising, as penetrating or perforating wounds which could involve directly the anterior portion of the calcarine region are very liable to injure at the same time the optic radiations. It is not uncommon, however, to find the so-called "telescopic vision" in patients who have been shot through the head in the lower parietal or temporal regions, as in the following case:—

Case 23.—Private F., 8,243, was wounded probably in the middle of June, 1915; he was unconscious for some days and was admitted to a base hospital on June 18.

Wound.—The entrance was 2 in. (5 cm.) above and $1\frac{1}{2}$ in. (3.75 cm.) behind the upper margin of the attachment of the right pinna; the exit was $\frac{1}{2}$ in. (1.25 cm.) above and $2\frac{1}{2}$ in. (6.25 cm.) behind the attachment of the left pinna. Both were small, punctured wounds. He was in a very drowsy and critical state when admitted, and had papillœdema with swelling of the discs of about 3D. and small hæmorrhages in their neighbourhood, but he improved rapidly after a decompression operation had been performed. The wounds healed rapidly and the papillœdema disappeared, but his vision was then found to be seriously affected. Six weeks after the infliction of the wound he could only read large letters, and his visual fields were limited to a zone of about 10° around the fixation point (fig. 27). He was able to recognize colours by macular vision. In this case measurements show the bullet probably passed the middle line of the skull, posterior to the splenium

and through the anterior part of the area striata, but as the optic radiations must have been also injured, the interpretation of his visual disturbance is doubtful.

It might, perhaps, still be argued that the evidence is not sufficient to conclude that central vision—that is, that subserved by the fovea

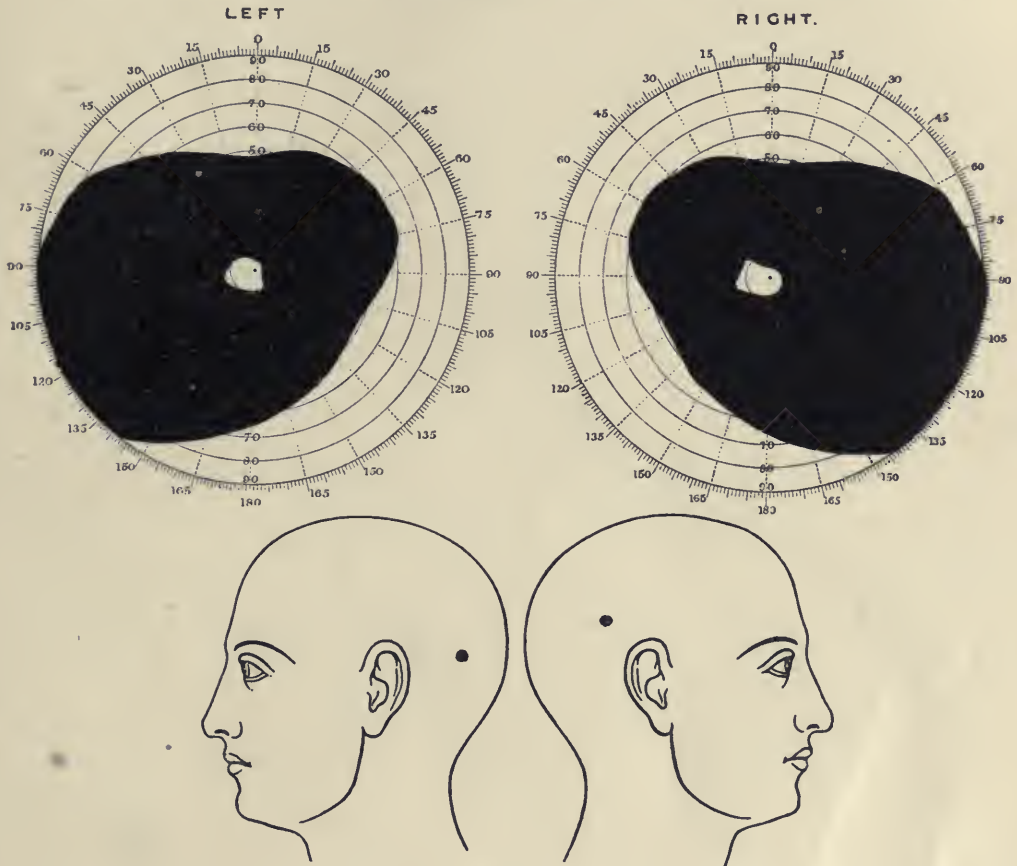


FIG. 27.

centralis—has not a double representation in the cortex, as certain of our fields may show that the blindness, whether in the form of a scotoma or of hemianopia, did not extend up to the fixation point; but we have found that the more exact the methods we employed, and the greater the care taken in making the observations, the nearer did the defect approach the fixation point. We consequently believe that, in common with every other part of the retina, the macula is not represented bilaterally.

In a certain number of the visual fields reproduced the areas of blindness are not quite symmetrical in the two eyes; in dealing with central scotomata this may be due to the obvious difficulty in obtaining central fixation, and in other cases to failure or fatigue of attention on the part of the patients suffering with recent head wounds. This tendency for attention to fail generally necessitates frequent short sittings in order to obtain accurate records.

Another point of interest is whether vision for colours may be dissociated from that for white—if, in other words, an achromatopsia may be produced by cerebral lesions. It is true that in certain cases we found the perception of colour lost in areas in which white was visible, but in such regions of the visual field vision even to white was indistinct and uncertain, especially when small test objects were employed. It consequently seems that loss of colour vision for objects of the ordinary test size (10 mm.) may be only a part of general reduction of visual acuity; we can, however, only state at present that we have no conclusive evidence that achromatopsia, with intact vision for white, is produced by cerebral lesions which involve either the cortex or the optic radiations.

Such observations as those we put forward here will be, no doubt, multiplied during the course of the War, and when finally collected should furnish fuller and more definite conclusions on localization within the cortical visual area. Inouye has attempted this from his observations on men wounded in the Russo-Japanese War, and Dimmer, Uthoff and Axenfeld have already described a certain number of important cases seen during the present conflict.

While this paper was in preparation the valuable and elaborate contribution of Pierre Marie and Chatelin to the same subject has come into our hands. We need only add that our work seems to be mutually confirmatory.

Our conclusions, which cannot yet be regarded as final, may be formulated concisely:—

(1) The upper half of each retina is represented in the dorsal, and the lower in the ventral part of each visual area.

(2) The centre for macular or central vision lies in the posterior extremities of the visual areas, probably on the margins and the lateral surfaces of the occipital poles.

(3) That portion of each upper quadrant of the retina in the immediate neighbourhood of, and including the adjacent part of, the fovea centralis is represented in the upper and posterior part of the visual area in the hemisphere of the same side, and vice versa.

(4) The centre for vision subserved by the periphery of the retinae is probably situated in the anterior end of the visual area, and the serial concentric zones of the retina from the macula to the periphery are probably represented in this order from behind forwards in the visual area.

Finally, it is our pleasure to acknowledge gratefully the help and assistance we have received from the medical officers of the various hospitals in which the patients were observed.

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A NEW FAMILIAL, INFANTILE FORM OF DIFFUSE BRAIN-SCLEROSIS.

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IN a previous paper [12], three years ago, I described a case of a peculiar affection in the brain of a child. This case I regarded as an early stage of the disease named "diffuse sclerosis of the brain," and in consequence of the characteristic histological findings I called this preliminary stage "perivascular necrosis of the medullary substance."

In the case in question the patient was but 1 year old, and it struck me that few cases in earliest infancy were to be found in international literature. Soon afterwards, however, I had an opportunity of seeing such a patient demonstrated, and after the death of the patient I was permitted to perform an autopsy and make a microscopic examination of the central nervous system.

The chief peculiarity of this case was its familial occurrence, which, at any rate from a pathogenetic point of view, rendered it different from all other cases described as infantile diffuse sclerosis. Further examination now showed that besides this case four other similar cases had been observed at the Dronning Louise's Boernehospital (Queen Louise's Hospital for Sick Children) and in the private practice of Professor Bloch—viz., the sister of the above-mentioned patient, two members of another family, and an isolated case. Two of these five patients have been demonstrated by Professor Monrad in the Pediatric Society of Copenhagen. Specimens from one of them, moreover, were demonstrated by Dr. V. Poulsen in the Section for Morbid Anatomy of the Biological Society. The third case had been briefly mentioned in the Pediatric Society by Dr. Joergen Bech and Dr. Monrad, and the two last cases during a discussion in the Pediatric Society by Dr. Bloch.

A thorough comparative and detailed report of these cases does not, however, exist, and the present paper may therefore be of some interest.

In the following paper infantile sclerosis of the brain alone will be

discussed, as, according to my view, the disease in children is somewhat different from that in adults.

I have much pleasure in recording my indebtedness to Professor Bloch and Professor Monrad for kindly permitting me to publish these cases. I am also indebted to Dr. V. Poulsen, who meant to publish the clinical history of two of the cases, but kindly left them at my disposal. Furthermore, I wish to thank Dr. K. Malling, who had prepared specimens from one of the patients, but generously handed the case over to me; and Professor Friedenreich, who permitted me to work out one of the cases at the Psychiatric Laboratory of the University (the main part of my investigation was carried out at the laboratory of the Children's Department of Rigshospitalet).

Case 1.—Kai Bn., son of a confidential clerk, born on November 25, 1912, died at thirteen months old. He was the second of a family of two; an elder sister suffered from the same disease, and is described below (Case 2). The father in his youth is said to have had hæmoptysis, the mother had always been healthy. Syphilis was denied. The patient was born normally at full time, the weight being at birth $3\frac{3}{4}$ kg. Up to the age of five months he developed fairly normally, was quick and gay, able to move his limbs freely. During the first four months he was suckled, but after that time was given milk-soup with bread and milk. When five months old he began to cry frequently and convulsively. At the same time fits of stiffness of all extremities appeared, with obstetrical posture of the hands and crossing of the legs. In the intervals between the attacks the patient was very weak and not able to sit up. The temperature was occasionally $38^{\circ}2'$ C. in the afternoon, but generally normal. The stools were mostly normal, and, except during the first months, there was neither regurgitation nor vomiting.

On July 7, 1913, the patient was admitted to the Queen Louise's Hospital for Sick Children, where physical examination gave the following result: Weight, 7,050 gm.; length, $62\frac{1}{2}$ cm.; circumference of the head, $43\frac{1}{2}$ cm.; circumference of the chest, 42 cm.; greatest circumference of the abdomen, 37 cm.; fontanelle, 3 cm. by 3 cm., normal tension; teeth, 0; temperature, $37^{\circ}3'$ C.; urine acid, turbid with urates, no pus nor albumen. The child was well nourished, sunburnt, normal appearance. Pupils large and active to light. No nystagmus. External examination of the eyes, ears and fauces showed no abnormalities; ophthalmoscopic examination showed greyish discs with veiled outlines (early optic atrophy). The patient followed things with his eyes. Slight universal micro-adenitis. Stethoscopic examination and examination of the abdomen showed no abnormality. No signs of rickets. Intense sweating. Violent crying and gasping during the examination. Body and limbs stiffly extended, head turned backwards, back crooked, hands often clenched, sometimes in tetanic posture; lower extremities strongly extended and adducted, toes spread (figs. 1 and 2). The examination of reflexes was difficult,

but Babinski's sign was present. During the examination attacks of convulsion occurred, which made the lower extremities still more stiff, head and back were drawn more backwards, arms moved up and down in clonic spasms. The fits were accompanied by convulsive crying and gasping. The attacks appeared without any obvious cause.

The course of the illness during the six months' residence was as follows: The Wassermann test on July 13 was negative; v. Pirquet negative. Lumbar puncture on November 10 showed about 3 c.cm. slightly turbid fluid, containing



FIG. 1.—Case 1, Kai Bn.



FIG. 2.—Case 1, Kai Bn.

a few endothelial cells but no other cells and no micro-organisms; there was no growth on agar, serum, bouillon, or ascites agar. The stools were nearly always normal even during the febrile periods. From July 23 to July 28 only were they found to contain some mucus, and on November 28 (during a period of fever) they were watery. There were, as a rule, one to three stools a day. Regurgitation occurred now and then, but no vomiting. The urine never contained sugar nor albumen, whereas on November 6 and the ensuing days

some pus was observed. When examined under the microscope (November 13) the urine was found to contain numerous leucocytes, a number of epithelial cells, and *Bacillus coli*, but no cylindrical cells or red blood corpuscles. The weight (on admission 7,050 grm.) increased during the first days some 100 grm., after which, during the following days, it dropped down to 6,300 grm. It then oscillated periodically between 6,200 and 6,800 grm., until it fell rather abruptly to 5,700 grm. The loss of weight, as a rule, appeared coincident with the febrile periods. The patient was fed at first on milk-soup and water (equal mixture), then pure milk-soup.

August 1: Patient sometimes dull, sometimes crying, falls into spasms at the faintest noise. Sleeps well at night; bathing appears to have a calming effect. He is able to follow movements with his eyes. No nystagmus. The stiffness of body and limbs unchanged.

August 25: Has gained in weight. Has been somewhat more quiet during the last days, but lies constantly in a spastic state; frequent exacerbations occur, in which his hands are clenched violently, arms moved to and fro, head drawn backward, and back crooked in arc de cercle, lower extremities extended, a slight indication of tetanic posture of the feet, no real nystagmus. The fits seem to cause pain, and are hardly followed by unconsciousness. In the upper extremities the reflexes are easily obtained, but ankle-jerks were not brisk. The knee-jerks were not obtained. Plantar reflexes normal.

December 1: Condition has grown worse, more difficulty in swallowing, and increased dulness.

December 29: Some cyanosis of the face since yesterday. No convulsions. Died at 12.30 p.m.

Dr. V. Poulsen, who saw the patient daily, characterized the case in the following way: An intense stiffness of all the extremities was observed during nearly all the time of residence in hospital. When examined, or when loud speaking took place in the room, he at once fell into tonic spasms. The dulness, however, did not appear until the last days, when he grew more debilitated, and the spasms were then excited only by stronger irritation. At the same time the eclamptic fits began, during which universal clonic and tonic convulsions appeared, combined with marked cyanosis.

It may be added that the elevations of temperature, before mentioned, were never followed by cough, dyspnoea, or other signs of pneumonia.

The clinical diagnosis was: sclerosis cerebri diffusa.

Post-mortem examination ten hours after death gave the following result: The body was that of a moderately nourished child; *rigor mortis* present. In both lungs extensive red, infiltrated, partly confluent portions of a typical pneumonic appearance. The mucous membrane of the bronchi hyperæmic. No signs of tuberculosis. Heart, stomach, intestines, liver, kidneys, spleen, pancreas, thyroid gland, and suprarenal bodies showed no abnormality. On opening the skull, theca and dura were found to be normal. From the subdural and subarachnoidal cavities a considerable amount of clear cerebrospinal fluid was evacuated. The brain occupied less room in the thecal cavity than is the

case with normal brains; its weight was 650 grm. Pia cedematous, not thickened nor of milky consistence. The ventricles of the brain were not distinctly dilated; no granulation of the ependyma. The consistence of the brain, cerebellum and spinal cord was found to be increased, so that the brain did not show any tendency to flow out after removal, as is generally the case with children's brains of that age, but kept its form, with medulla oblongata protruding into the air. The increase of consistence was most pronounced in the cerebellum and medulla. On the cut surface the cortex appeared to be soft without any abnormality, the medullary substance was harder and, especially in the most central parts, greyish-red, but whitish in the thin subcortical layers.

Blocks were immediately taken for microscopical examination, hardened in 96 per cent. alcohol, Müller's fluid, Weigert's stain for neuroglia, and 10 per cent. formaldehyde respectively. Some of the pieces hardened in formaldehyde were later on prepared in Flemming's fluid. The rest of the brain was kept in 4 per cent. formaldehyde and after some months large slices (transverse sections) were transferred into Weigert's brown chromic acid stain. The following methods of staining were carried out: Nissl's thionin staining, Weigert-Kulschitzky-Wolters method, and Spielmeyer's method of staining for medullary sheaths, Marchi's staining, Bielschowsky's staining, staining of the fat with Sudan red, Alzheimer's method of staining for neuroglia with Mallory's hematoxylin, and Alzheimer's acid-fuchsin—vert-lumière staining. The last method especially gave fine glia pictures. As in my previous work on sclerosis of the brain, I have here embedded in paraffin at low temperatures.

Microscopic examination gave the following result:—

The hemispheres of the cerebrum.—The pictures of the medullary sheaths (stained by Weigert-Pal) show to the naked eye an enormous destruction, so that the white matter is found to be almost as pale as the cortex (fig. 3). Immediately under the cortex only a narrow streak (1 cm. to 2 cm. in width) of darker stained tissue is visible. Under the microscope, however, the destruction appears to be not quite total: a scanty number of medullated nerve-fibres are found crossing in all directions. The destruction of the medullary sheaths in the white matter is not quite evenly distributed, and a thin layer of much less destroyed tissue is found in the peripheral regions. In addition, the central part of the white matter contains small scattered islets of totally destroyed tissue, while the surrounding plexus is relatively less destroyed. On the whole, the destruction increases towards the centre. The areas around the smallest vessels are, as a rule, not specially affected by the destruction, while the bigger ones are surrounded by a thick border of totally destroyed sheaths. In the cortex, on the other hand, slight wasting only of the medullated fibres is traceable; both tangential

fibres and supra- and inter-radial fibres are present, although somewhat more scanty than usual.

In large sections (fig. 3) of the brain stained by the method of Kulschitzky-Wolters and Pal the process was found to be uniform throughout the whole cerebrum, and no normal white matter was left except the thin subcortical layer, which was everywhere preserved. In Marchi specimens only a very small number of blackened granules are found in the white matter and in the cortical substance. In the big cells which surround the vessels and fill up the vessel sheaths only small collections of cells are occasionally observed, the granules of which are blackened with the osmic acid.

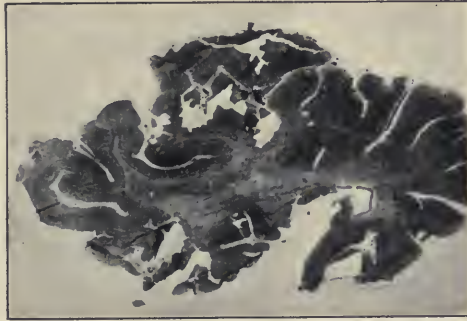


FIG. 3.—Section from the occipital lobe of the brain of Case 1, Kai Bn. Staining of Weigert-Pal. The black line between the cortex and the medullary substance represents the only remains of the white substance, the lighter part inside this line is medullary substance, which is replaced by neuroglia and therefore uncoloured.

Bielschowsky specimens show an immense destruction of the axillary cylinders corresponding with that of the medullary sheaths, so that only a small number are found to radiate widely, and even these are to some extent in granular decay. In the cortex, however, the nerve-cell processes seem to be quite as numerous as in a normal brain, although some of them are in granular decay and irregularly thickened, possibly due to *post-mortem* changes. Cajal's corpuscles cannot be observed.

The specimens stained for neuroglial changes clearly illustrate the positive corresponding with the negative findings of the medullary sheaths. In specimens stained with acid-fuchsin—vert-lumière (figs. 12 and 13, pp. 104, 105) a red substance is visible to the naked eye, corresponding with the white matter. When examined under the microscope this substance is found to consist of glia-fibres, the number and density of which are fairly uniform throughout the whole field of view. In a thin layer surrounding some of the largest vessels, the glia-fibres, however,

seem most closely packed together, taking here the same longitudinal direction as the vessels. Among the glia-fibres cells of very different shape and size are traceable. Some of them are small and mononuclear, containing but a very thin protoplasmic layer. In other cells the protoplasm is of almost gigantic dimensions, forming a roundish or irregular outline, sometimes homogeneous, sometimes slightly granular, with big vacuoles or recesses. Between these cells and the smaller ones transitional forms are found, mostly irregular or lobed in outline. The contents of chromatin of the nuclei varies greatly: the bigger the cell, the more scanty the chromatin. The nuclei generally contain one or two nucleoli, and as a rule are arranged excentrically. It is not, however, evident from these glia pictures whether or not the cells are sending out processes, while in specimens stained by Alzheimer-Mallory's method (fig. 16, p. 107) cell processes enclosing the glia-fibres are distinctly visible. On the other hand, the typical amoebic glia-cells are here extraordinarily few in number. The distribution of cells is fairly uniform throughout the glia substance; in the outer subcortical layer perhaps the number may be somewhat smaller than in the central regions round the vessels, where the bigger glia-cells are replaced by cells which fill up the adventitia sheaths of the blood-vessels (fig. 13). A great number of these cells have a large round protoplasm, similar to that of the bigger glia-cells; they are, however, more degenerated and contain pale homogeneous nuclei and nucleoli which have entered the protoplasm, and finally oblong cells which seem to fit into the shape of the vessel sheaths. Granules stained by osmic acid are, however, of very rare occurrence in these cells. On comparing these specimens with those stained with Sudan red only a very small number of them will be found to contain fatty granules. This is quite in keeping with the pictures of the medullary sheaths, where only very few bluish-black granules are found in the cells. It may be added that the vessel sheaths only contain these "empty fatty granule-cells" and "scavenger cells" (Alzheimer's *Abräumzellen*), and nowhere any sort of inflammatory cells—in fact, neither plasma-cells lymphocytes, nor polymorphonuclear leucocytes.

In the cortex the condition is quite different to that of the white matter. The outer glia is hardly thickened, and only occasionally in the cortex itself a single thread-forming glia-cell (*see* fig. 14, p. 105) may be observed. The vessel sheaths nowhere contain scavenger or other cells. The boundary between cortex and the white matter stands out rather distinctly in the glia pictures macroscopically. On microscopic examina-

tion, however, a transitional region is observed in which the number of glia-fibres and cells is seen to decrease towards the cortex. This region apparently corresponds with the thin layer of preserved medullary sheaths. In specimens stained by Nissl's method, protoplasmic glia is found corresponding with the white matter, and scavenger cells similar to those mentioned above. More distinctly than in the real glia pictures, these specimens present small, intensely stained corpuscles resembling the calcareous concretions of the meninges and pineal gland arranged round the blood-vessels. The nerve-cells of the cortex apparently show no abnormality; the condition of the Nissl granules cannot be made out definitely, as the *post-mortem* examination was not carried out till ten hours after death; at any rate, no important Nissl changes can be seen. The appearance of the nuclei is normal, there is no pycnoid change of the protoplasm, and no abnormal number of big cells. On the whole, no destruction of the nerve-cells can be seen.

In some places the pia appears to be somewhat thickened and rich in cells, but is nowhere infiltrated. The vessels of the cortex are normal, whereas those of the white matter at the first glance look pathologically changed. When examined more closely, the intima and media, however, appear to be normal, and the changed appearance of adventitia is due to the great number of scavenger cells.

The *mid-brain* shows on the whole the same changes. The destruction of the medullary sheaths, however, does not seem quite as extreme as that of the hemispheres, and apparently diminishes towards the pons. Marchi degeneration cannot be seen, and fatty granules are only rarely visible. The destruction of the axis-cylinders of the white matter seem to be parallel with that of the sheaths. The nerve-cells of the great ganglionic centres present a similar appearance to those of the cortex. In the nuclei of the cranial nerves the Nissl pictures show unchanged nerve-cells; distinct Nissl granules are seen, and there are no acute changes. A glial increase is seen in the mid-brain similar to that of the hemispheres, although somewhat less sharply limited, and similar glia-cells and scavenger cells are traceable. Furthermore, pathological changes are seen similar to those found in gliomata (*see* fig. 15, p. 106), gigantic cells with a large, irregularly outlined protoplasm and several nuclei placed peripherally or embedded in niches. In addition to these, a number of smaller cells with degenerated nuclei and thick protoplasmic processes are found. Among these cells a multitude of processes are seen crossing each other obliquely; or in some places showing a parallel course. Among these thicker fibres, ordinary thin glia-fibres

are noted, and finally in addition transitional stages. The giant-cells, which at the first glance had some resemblance to degenerated nerve-cells, are pathological forms of glia-cells if anything, as some of the processes are found to contain glia-fibres.

Cerebellum.—In specimens showing the medullary sheaths a still greater destruction is to be seen, which does not decrease in the most peripheral part of the white matter. In the grey matter also destructive processes are observed, proportionately less marked in the stratum granulosum. Marchi degeneration is nowhere traceable. The axis-cylinders are somewhat better preserved than the myelin sheaths. In the glia specimens the white matter is seen to be replaced by dense fibrillar glia, containing both big and small glia-cells. The increase of glia, however, is not only found in the white matter, but also in the granular layer, and even in the molecular layer, where some isolated glia-fibres passing radially are seen. The vessel sheaths contain scavenger cells, in some places filled with fatty granules. The stratum granulosum does not show anything particular in the Nissl specimens, whereas Purkinje's cells appear to be somewhat shrunk and seem to have somewhat defect processes.

Bulbus olfactorius was examined by Nissl's method only; no prominent changes of the cells nor infiltration of the vessel wall can be observed.

In the *tractus opticus* and *chiasma* an intense destruction of the medullary sheaths is seen, especially perivascular, around the vessels; rarely the denser bundles are preserved. Except in some places around the vessels the axis-cylinders have also been destroyed for the most part, corresponding with the regions where the medullary sheaths are totally destroyed. Corresponding with the destruction of the myelin sheaths, an immense number of glia-fibres and cells are seen, showing the same appearance as those of the hemispheres. In the adventitial sheaths of the vessels and round the vessels, scavenger cells and fatty granule-cells are of very rare occurrence.

The spinal cord and medulla oblongata.—Throughout all the sections of the spinal cord a diffuse destruction of the medullary sheaths is to be found in the white matter. It is most advanced in the pyramidal tracts, which at this period of life ought to be developed and least pronounced in the root entrance zones. In the grey matter no signs of destruction can be seen. The Marchi degeneration is just as scanty as was the case in the cerebrum. The destruction of the axis-cylinders seems less pronounced than that of the sheaths. In the pyramidal

tracts, however, very few axis-cylinders are present. The grey matter shows a fine figuration of axis-cylinders and of the intercellular fibrillæ. Corresponding with the destruction of the medullary sheaths a very conspicuous proliferation of the glia is observed. In the outer parts are seen strong radial projections, among which lie a scanty number of fibres, crossing into all directions. Among the glia-fibres cells are observed of very varying appearance, as was the case in the brain. The glia has no particular relation to the vessels. The adventitial sheaths are usually filled with big scavenger cells, which in specimens stained with Sudan red appear to contain no fatty granules at all.

In the grey matter no glia increase is found, and there is no abnormality in the tissue surrounding the central canal. Here, too, the nerve-cells appear to be preserved and the Nissl's figures and neurofibrillæ are clearly defined and normal.

Case 2.—Bodil Bn., daughter of a clerk, was born on February 21, 1911; died at the age of 1 year. The patient, the elder sister of the first patient, was born normally at full term. The weight at birth was 4 kg. It was noticed by the midwife that the child was unusually stiff, and immediately after birth rigidity of the nape of the neck was discovered. Up to the age of four months she was suckled; then she was given barley broth, milk, water-gruel, Nestlé's food, and unboiled milk. The patient, however, after weaning had fits of crying and frequent vomiting, which abated as soon as the patient was put upon buttermilk. She was often slightly febrile for a few days in succession. Development proceeded normally until the fourth month, after which she did not advance mentally and was hardly able to recognize her mother. The stiffness of the neck and legs continued, and the fits of crying were spasmodic, accompanied by severe congestion, but regular convulsions did not occur.

On November 7 she was admitted to the Dronning Louise's Boernehospital (Queen Louise's Hospital for Sick Children), and physical examination there showed: weight of body, 4,700 grm.; length of body, 64 cm.; circumference of head $40\frac{1}{2}$ cm.; circumference of the chest, 39 cm.; greatest circumference of the abdomen, 31 cm. The expression was rather stupid and vague, the cry hoarse and convulsive. The pupils were active to light. The child was lying stiffly bent backwards, with marked opisthotonos and strong lordosis of the lumbar region. Universal rigidity of the muscles was most pronounced in the lower extremities, which were hyperextended and adducted. Hands and feet were in the tetanic posture. The appearance of skull and eyes normal. Ophthalmoscopic examination (September 9) showed the right disc white and atrophic, the left pale. Fauces normal; stethoscopic examination normal; abdomen somewhat contracted (figs. 4 and 5).

The patient seemed conscious and sensitive to pain. Examination ten days later showed almost continuous tonic rigidity of all muscle groups

combined with the tetanic posture. Now and then periods of violent spasm appeared, especially in the lower extremities and in the back and neck, so that "arc en cercle" appeared. Nystagmus was sometimes present. The pupils reacted rather slowly to light. She never smiled, never seemed to be conscious. The fontanelles were large and sunken. The plantar reflexes brisk, but of uncertain form. The patellar reflexes could not be obtained on account of the rigidity.



FIG. 4.—Case 2, Bodil Bn., aged 7 months.



FIG. 5.—Case 2, Bodil Bn., aged 7 months.

Examination of the organs showed nothing abnormal. No rickets. Wassermann's test (October 19) negative; v. Pirquet (September 17 and October 10) negative.

As to the course of the illness, the following facts were stated: The temperature was normal at first; after a fortnight slight elevations (to 38° C.) were noted during the following week. Then again a week passed with normal temperature, succeeded by a febrile period.

Up to October 27 the temperature remained raised, but then became normal again after a week. Then it ran an irregular course ranging between normal

and 38° C.; for a few days a subnormal temperature was noted, then again a normal and slightly raised temperature alternately. For about a fortnight from December 21 the temperature remained normal or subnormal, and then after a short febrile period began to oscillate between 34° C. and 38·3° C.

The stools were normal throughout, except on one day. In the beginning there was frequent vomiting, which later occurred once or twice a day. In the last month vomiting did not occur at all. The urine contained traces of albumin and epithelial cells, urates, a number of cylinders, but no leucocytes. No growth occurred. On later examinations it did not contain albumin. The weight on admission was 4,700 grm., was steadily increased during the following months up to 5,600 grm., then decreased during the next month, until at last it fell rather abruptly to 4,800 grm.

The patient was given buttermilk for the first two days, and after this milk and barley water in equal parts seven times a day; this was increased to pure milk 150 grm. seven times a day.

Her progress was as follows:—

October 18: Patient drinks well; good stools; has gained in weight; condition all but unchanged, more or less spasmodic, sometimes interrupted by violent tonic spasms, which are nearly always accompanied by screaming. These attacks are evidently very painful, and are roused by the faintest influence from without, as, for instance, by sudden light or touch. More marked nystagmus than before. Corneal reflexes scarcely obtained, the pupils are but slightly active to light. Circumference of head, 42 cm.; circumference of chest, 39½ cm. The fontanelle: 3 cm. by 3½ cm., distended only during the attacks. Regurgitation and vomiting are frequently reported. Action of the heart regular.

October 28: Drinks poorly, condition much worse since the last note, scarcely any reaction to noise, attacks produced only when she is touched. Vomiting again of frequent occurrence.

January 13: Previous fits of crying all but ceased; very insignificant spasmodic stiffness. Plantar reflexes still rather brisk, most of the other reflexes abolished. Nystagmus rarely observed. During the last few days difficulty in swallowing has supervened.

February 6: Patient is lying unconscious, not able to swallow. Died at 8 a.m.

Post-mortem examination, nine hours after death (Dr. Oerum), gave the following results: Small scattered, apparently hypostatic, pneumonic patches, but no other special abnormality; no signs whatever of lues.

The most conspicuous pathological changes were found in the central nervous system, examined by Dr. Malling, who has given the following description: The brain and the spinal cord, in contradistinction to the soft, nearly confluent central nervous system generally found in children, is solid and hard and keeps its shape. There is no difference as to hardness between different regions; the sclerosis is diffuse and affects the cerebellum and the mid-brain. The gyri throughout the brain stand out distinctly and are

unusually small and slender. The nerves of the base, especially the optic nerves, are solid, hard, and thickened. The pia is somewhat thickened and indistinct. The cortex is of normal colour and depth, and immediately under it a streak of normal white medullary substance (2 mm. in width) is seen, but more centrally the white matter presents a peculiar greyish translucent colour, the knife passes easily through the cortex, whereas the rest of the substance of the brain is tough and hard to cut.

Sections were made from the frontal and occipital lobe, from the gyrus paracentralis, from the cerebellum, and from the dorsal, cervical and lumbar regions of the spinal cord, the optic and facial nerves. The following methods of staining were pursued: The ganglion cells were stained with thionin (method of Nissl), van Gieson, Weigert's staining for elastine and for neuroglia, Kultschitzky-Wolters' staining for medullated nerves, Marchi staining and Bielschowsky's method of staining for neuro-fibrils, various methods of staining glia (Alzheimer), Levaditi's silver method of staining spirochaetes.

Dr. Malling's description of the microscopical examination is as follows. To this, after having re-examined the specimens, I have added some supplementary notes in parentheses.

Cerebrum.—Pia appears to be somewhat thickened, especially above the motor region, but no great infiltration of cells is traceable. Most of the cells are fibroblasts and fatty granule-like cells. No plasma cells. (The thickening seems to be due essentially to oedema.) On examining under low magnifying powers specimens of the brain stained with thionin, the cortex is found to be, on the whole, fairly well preserved; it contains the usual layers of cells, but in the motor region the giant pyramidal cells are diminished. Just inside the cortex a light zone is seen, visible also to the naked eye, which contains a few cells only; more centrally, the whole white substance stains intensely, the colour increasing towards the centre. The most prominent feature of this zone is a multitude of blood-vessels, surrounded by large intensely stained cells, and it is clear that the main incidence of the process falls upon the vessels. Under high magnifying powers a chronic inflammation of the ganglion cells is seen, the nuclei are diffusely stained blue, the protoplasm is in granular destruction, otherwise the cortex appears to be quite normal. There is no noteworthy increase of the glia, nor any new formation of the vessels. No cells of infiltration. In the more highly stained zone, just internal to the cortex, no abnormality of the vessels can be seen; as a rule polynuclear glia-cells are visible. Still more centrally in the white matter a confusion of various cell forms appears. On examining a typical blood-vessel the lumen is not particularly diminished, and is as a rule empty; then comes the endothelial

layer with nearly normal cells and without any special proliferation; then, in most cases, a more or less light zone. But as soon as we reach the adventitia and perivascular region an enormous proliferation of large epithelial cells is observed, felted together and more or less angular, in contradistinction to the round cells of the tissue. These cells often contain a number of nuclei, peripherally arranged and always degenerated. The protoplasm is stained diffusely, and, in some of the cells, large dark clumps, like degenerated nuclei, are found. The said cells are placed in one or several layers round the vessel. The tissue contains similar cells, the dimensions of which are often gigantic, but they seem here more prone to vacuolar degeneration; sometimes they contain several small, sometimes one big vacuole, and thus perhaps are transitional stages to the real fatty granule (basket?) cells. The latter are found in great numbers in the tissue or in some of the vessel sheaths, as may be seen from the Marchi specimens (black-stained lipid grains). The large cells mentioned above do not contain lipoids. In addition to these cell forms, a number of small dark nuclei with a scanty and somewhat tattered protoplasm are noticed in the glia-cells. Some of the vessels are apparently normal. The above changes are also present in the frontal, occipital and paracentral gyri.

In specimens stained for medullated nerves, scanty remnants only of the sheaths are traceable. The tangential and supra-radial fibres appear to have been completely destroyed, possibly owing to a too strong differentiation, and in the central part of the white matter there are practically no fibres; whereas, corresponding to the above "light zone," immediately under the cortex some fibres are seen, although they are considerably degenerated.

So much for the frontal and paracentral gyri. In the occipital gyri more fibres are found, and the zone of Baillarger is extraordinarily well preserved. As a sort of compensation for this almost complete destruction of nervous substance in the white matter, specimens stained for neuroglia by Weigert's method show an enormous proliferation of the glia to a degree that cannot be equalled in any other affection of the brain. The number of glia-nuclei is rather small in proportion to the glia-fibres. The fibres are, as a rule, thin and slender. In contradistinction to this enormous subcortical gliosis no increase worth mentioning is found in the cortex or marginal glia.

Similar changes are observed in the cerebellum. In the central part of the white matter the cells and changes are exactly the same as in the cerebrum; they decrease towards the granule layer, which is less

compact than usual and swarms with a number of cells, evidently glia-cells. The cells of Purkinje are somewhat degenerated and the medullary sheaths are totally destroyed, but for some few traces in the granule layer. Small bundles of medullary sheaths are also found to be intact in the white matter. In specimens stained by Bielschowsky's method, it is seen that the axis-cylinders are also destroyed. In the cerebellum also the degenerated nerve tissue has been replaced by glia, which stretches into the granule layer and runs as fairly parallel fibres right through the molecular layer to the surface (Bergmann's fibres).

The optic nerve and, to some extent, the facial nerve show more or less complete destruction, the former being transformed into glia tissue.

The cervical spinal cord, when examined in thionin specimens, appears to be somewhat effaced, so that the line of demarcation between the grey and the white matter is not easy to make out. In the grey matter large portions, especially the anterior horn-cells, are destroyed. This, however, is in our opinion somewhat doubtful, as the large motor cells of the anterior horn are also extraordinarily well preserved. All through the grey and white matter a conspicuous new formation of blood-vessels is observed, and cells similar to those of the brain, with vacuolation and a multitude of glia-cells, are present. In specimens stained for medullated nerves the whole transverse section of the spinal cord appears to be greatly degenerated, although not quite uniformly; the grey commissure, the spinal cerebellar tracts and the root-zones are the best-preserved portions, the anterior and Burdach's columns are moderately degenerated, and Goll's columns and the pyramidal tracts are completely destroyed. The fibres of the grey matter are much degenerated. In glia specimens the enormous marginal gliosis sending out thick glial septa into the substance is the most dominant feature; for the rest, the glia tissue is strongly increased throughout the transverse section.

Changes similar to these are found in the dorsal and lumbar cord. In the dorsal region the degeneration of the medullary sheaths is found somewhat more centrally in the posterior column, whereas in the latter place moderately preserved spinal cerebellar columns are not observed. In the cervical and less distinctly in the lumbar cord, in front of the central canal, a rather deep lateral fissure and several smaller fissures are noted.

Weigert's elastic tissue stain does not show any pathological changes in cerebrum, cerebellum, or in spinal cord.

Levaditi's silver method for staining spirochætes gave a negative result.

On the whole, stained specimens from this patient present much the same pictures as those of Case 1, the essential difference being, in my opinion, that the scavenger cells of the vessel sheaths in Case 2 are found to contain far more fatty substances than those of the previous case. It may be remarked that no inflammatory processes were found in these specimens, any more than in those from Case 1.

Case 3.—Agnes A. B., daughter of a bricklayer, born October 10, 1904, died in the Dronning Louise's Boernehospital (Queen Louise's Children's Hospital) at the age of nine months.

The patient was the eldest child; her younger sister is described as Case 4. She had a convergent squint from birth. She was brought up on the breast and thrived well, except for the stools, which were green; this caused the mother to apply to the polyclinic of the hospital. The meals were regulated, bismuth was given, but the stools remained unchanged. At the age of five months attacks of diarrhœa occurred, and a week later stiffness of the body with opisthotonos and violent screaming. Patient took fluid food poorly, vomiting being rather frequent.

On April 5, 1905, she was admitted to the hospital and physical examination showed: weight, 4,358 gm.; temperature, 37.5° C. She was a slender, well-nourished child. Stethoscopic examination normal; ears and fauces normal; a small umbilical hernia was noted; the fontanelle was not distended, but if anything somewhat sunken. Strabismus convergens present. No facialis or Trousseau's symptoms. During examination there were frequent attacks of total stiffness of the body and extremities, followed by opisthotonos; the arms were flexed at the elbow-joint, fists clenched with the thumb partly within, partly outside the other fingers. The lower extremities were extended and the feet in plantar flexion. Nystagmus of both eyes; patient yawned often and violently, smacking her lips now and then; colour did not change. The stools at first were thin, greenish, acid, aromatic-smelling, then mucous with an alkaline reaction. When examined under the microscope they were found to contain only mucus and a few decaying cells (epithelial and pus). The stools remained thin and mucous; on repeated examination (February 15) a few fatty acid crystals and mucus with a few cells were noted. During the whole residence in the hospital the stools remained mucous and thin in spite of change of diet. Vomiting was of almost daily occurrence and regurgitation very frequent.

The weight on admission, 4,350 gm., in the following fortnight was increased to 4,600 gm., after which it dropped down to 3,400 gm. During the last time again it rose to 3,900 gm. Lumbar puncture gave a negative result. The urine passed was scanty on April 9, 10, 11, but later became abundant, and on April 9 was slightly turbid, contained a slight amount

of albumen and no sugar. On ensuing examinations albumen was sometimes found, sometimes not. The fontanelle remained retracted during the whole stay in hospital. The patient was given the breast once or twice a day, and besides that barley water without admixture at first, then with milk, later on buttermilk soup, children's food, Liebig's soup. Her progress was as follows:—

April 10: Stiffness not diminished; this morning transitory clonic spasms of the lower extremities. More willing to take her food, has sometimes taken fluids well. Somewhat more lively. In the left half of the mouth a considerable reddening of the mucous membrane is found, and on the left side of the palate in the sulcus alveolo-lingualis yellowish mucous projects, which can be removed without difficulty.

April 16: During the last twenty-four hours some convulsive attacks. The patient is rather cold.

April 17: Drinks well. No convulsions, no stiffness of arms and legs. The nape of the neck is now and then drawn backwards, but the spinal column is not stiff. The mucous membrane of mouth and throat clean, red, moist; the palate wound is healing up.

April 19: Again frequent crying. Spastic rigidity of body and extremities. The patient looks very pale. The mucous membrane of the mouth dry, red; here and there ulcerated. Skin elastic.

April 23: Spastic stiffness, slight convulsive spasms of the lower extremities. Condition on the whole unchanged.

April 25: Oedema of hands, feet and thighs.

April 29: Yesterday afternoon one attack of clonic convulsions in the arms and tonic stiffness of legs and spinal column. The nape of the neck bent backwards. Consciousness preserved, no crying, sweating, or congestion during the fits. Occasional nystagmus has been noted. The lower extremities stiffly extended, nearly hyper-extended in the knee-joints. Arms stiffly flexed. Spine not rigid. Oedema of the back of the hand. In the lower extremities scarcely any oedema.

May 7: Dozing; cries only when touched. The lower extremities stiffly extended. In the bath this morning opisthotonos was noted for a moment. No clonic convulsions or laryngeal spasms. Hands cold, otherwise warm. Abdomen somewhat extended in the epigastrium, else otherwise soft; no visible peristalsis, the stomach cannot be marked out.

May 13: Permanent rigidity of legs and spinal column. Heart sounds faint and low.

May 23: Is lying quietly, only wails when touched; is still able to take the bottle; keeps fairly warm. Abdomen intensely sunken. Opisthotonos in the bath, not otherwise. The lower extremities stiffly extended. Some squinting. Scanty secretion from conjunctivæ. Dorsal kyphosis and lumbar lordosis more pronounced than before. In heart and lungs no abnormality. Perpetual yawning.

May 27: Extreme emaciation. Lower extremities constantly stiffly

extended, arms stiffly flexed, nape of the neck bent backwards. Abdomen flattened in the lower part. Epigastrium sunken. On examination the lungs are normal. Heart sounds strong and normal. No hæmorrhages anywhere. No conjunctivitis.

June 6: Œdema of both hands.

June 7: No thrush during the last days. Slight œdema of the upper part of the foot and of thighs. Lower extremities stiffly extended at the hip- and knee-joint. The legs are kept parallel, tightly pressed against one another, and cannot be abducted nor bent passively. Sometimes they are crossed at the ankles. The ankle-joints are slightly plantar-flexed, and the toes, especially the big toe, strongly flexed. The arms are kept at a distance from the body, slightly bent in the elbow, pronated, with the hands dorsally flexed and the fingers tightly clenched into the fist. The thumb is placed at the side of the other fingers. The rigidity of the arm muscles, however, is not so completely wooden as that of the legs. The degree of flexion varies. The spinal column has throughout been intensely arched: a dorsal kyphosis with a corresponding lumbar lordosis. The nape of the neck is stiff and the head is bent backwards, sometimes slightly, sometimes more considerably. The fontanelle is somewhat retracted. Now and then convergent strabismus is present. Some nystagmus. The pupils are equal, of moderate size and active. Perpetual intense yawning, which causes a subluxation of the jaw-joint. No clonic convulsions, no laryngeal spasms. No affection of the face. Abdomen formerly contracted, now rather tympanitic and distended. Taches cérébrales only just traceable. In spite of the evident emaciation she had gained 500 gm. in weight during the last ten days. Pulse not palpable. Heart sounds scarcely audible. Suggillations in the abdominal wall. Ophthalmoscopic examination normal. Left pupil bigger than right.

June 8: Difficulty in swallowing. Discharge of urine ceased. Rigidity as before, spasms did not occur. Died quietly at 8.30 a.m.

Post-mortem examination six hours after death gave the following results:—

An abundance of clear serous fluid was found in the subcutaneous tissue and in all serous cavities. The posterior parts of both lungs, especially the upper lobes, were infiltrated and collapsed. The bronchial and mesenteric glands not swollen. The mucous membrane of the digestive tube seemed normal; no hæmorrhages or swelling of Peyer's patches or of the follicles, which were not even visible. Œsophagus coated with a thick layer of thrush. No thrush in stomach or mouth. Heart, liver, spleen and kidneys were small and normal. The epiphyseal lines of the ribs normal. Spinal cord normal to the naked eye.

The pia and arachnoid were œdematous, but no distinct exudate was found. The gyri were very little flattened. Both lateral ventricles were greatly dilated and separated from the surface by a thin layer of brain tissue only (about 3 cm. to 4 cm.). The cerebellum was small, and in consistence cartilaginous. The rest of the brain, was, if anything, soft.¹ On the cut surface the glia

¹ Regarding this point some divergence of opinion appears. The account of the autopsy was written to the dictation of the then (now deceased) chief physician, Dr. Wichmann,

tissue of the latent lobes seemed to be increased (the brain was sent to the Anatomical-Pathological Institute of the University of Copenhagen).

Case 4.—Gudrun Marie A. B., daughter of a bricklayer, born 1905, died February, 1907.

According to information from Dr. Kiær, in Hammel, the child, when visiting Hammel, was suffering from constipation. She is *the younger sister of the above patient*, was never admitted to the hospital, but treated at home by Dr. Bloch, who has given the following information:—

The disease was similar to that of her elder sister. The child was normal during the first months of her life, but then began to suffer from stiffness of the extremities and tonic cramps. Ophthalmoscopic examination was not undertaken. Frequent periods of elevated temperature occurred, during which the cramps grew stronger and the patient more debilitated. No stethoscopic changes nor intestinal symptoms were discovered during these periods of elevated temperature; on the other hand, vomitings were of frequent occurrence throughout the disease. She lived somewhat longer than the other patients and was $1\frac{1}{2}$ years old when she died.

The parents taking an interest in knowing whether or not the child had suffered from the same affection as her elder sister, Dr. Bloch was permitted to perform the autopsy at the home; the result was as follows:—

Brain (figs. 6 to 7) and spinal cord remarkably hard, almost cartilaginous, but did not present any abnormal configuration. The brain was placed in formaldehyde. When examined now (seven years later) the brain showed the following appearance to the naked eye: it was normal in shape and showed no macroscopic defects. It deserves to be mentioned that the shape had been so perfectly preserved that the organ had not flowed out by its own weight, as is usually the case with children's brains, but had remained remarkably hard, even before fixation. On the photograph (figs. 6 to 7) it is seen that the medulla oblongata straddles in the air, an unusual condition for a child's brain. On palpation the consistence of the cortex is found to be normal, whilst the white matter is extraordinarily hard—much harder than usual in a brain hardened in formaldehyde. This hardness is uniform throughout the organ. On the cut surface the cortex appears to be of normal colour and thickness, and is distinctly marked off towards the white matter, which is apparently somewhat diminished and of a reddish, somewhat marbled, grey colour. Immediately under the cortex lies a thin layer of substance which is still white.

whilst the then assistant physician, Dr. Bloch, also took part in the autopsy. He informs me that, according to his view, the rest of the brain was also extremely hard, though not quite as hard as the cerebellum. There is, on the whole, some reason to suppose that the process was not quite so far developed in this case as in the four other cases, as evidenced by the following circumstances: (1) the normal ophthalmoscopic appearances; (2) the severe gastro-enteritis, which in all likelihood caused the death at an earlier point of time than in the other cases.

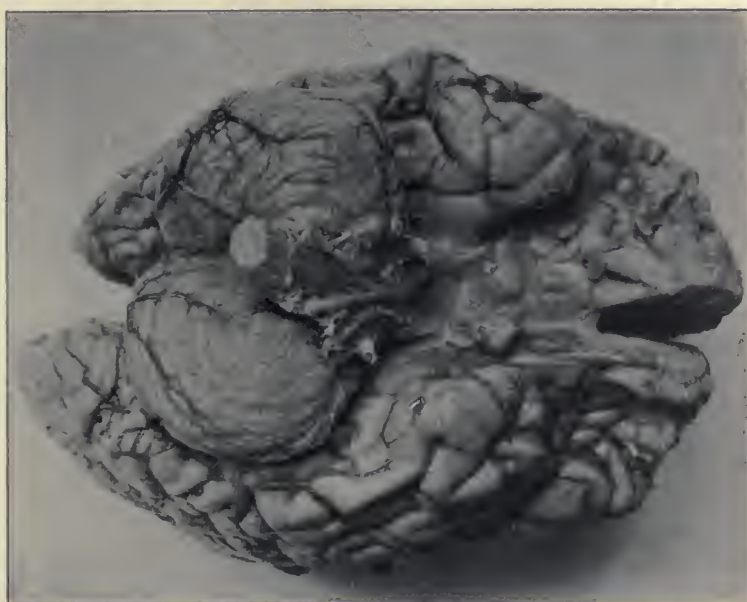


FIG. 6.—The brain of Case 4, Gudrun A. B.



FIG. 7.—The brain of Case 4, Gudrun A. B.

Pieces of the brain were prepared: smaller sections for transference into chrom-acid acetic-acid mixture for the purpose of acid-fuchsin—vert-lumière staining, and larger slices, which were treated with Weigert's brown chrom-stain, and stained according to the methods of Kulschitzsky-Wolters and of Pal. When examined under the microscope these specimens, representing all regions of the brain, were found to contain changes (figs. 8 to 10). The white matter of the cerebrum, excepting a thin subcortical layer, was almost completely destroyed. The nerve-tracts in the pons were fairly preserved. Corresponding with the destruction of the medullary sheaths, an enormous increase of glia-tissue with large protoplasmic glia cells and infiltration of the vessel sheaths with scavenger cells was seen. As in Case 2, these cells for the most part were filled with fatty granules.

Case 5.—Frederik Ernst Ed., son of a baker, born October 12, 1905, died at the age of 11½ months.

Family history: Parents healthy, patient second of a family of two. The elder was healthy (according to later information subsequent children were also healthy). The patient was fed on nothing but the breast until admission to the hospital. During the first three to four months he was fairly well and thrived well. Then for some time he began to suffer from constipation; a fissure of the anus necessitated division of the sphincter. After this his condition improved and stools occurred spontaneously. Shortly afterwards, however, attacks of screaming and tetanic rigidity of the upper and lower extremities appeared. Now and then there was transitory elevation of temperature. Patient looked dull, and there was a peculiar smacking and masticating motion of the mouth, and moving of the tongue forwards and backwards. Examination of the chest and urine showed nothing abnormal. At the age of 6 months a kyphosis appeared in the dorsal region. The patient grew somewhat more quiet, but was admitted to Dronning Louise's Hospital (Queen Louise's Hospital for Sick Children) on May 23, 1906.

Physical examination then showed: Weight in full, 5,050 gm.; circumference of head, 43 cm.; circumference of chest, 38½ cm.; temperature, 37.5° C.; pulse 140. Urine contained much urates, but no albumen nor sugar. State of nutrition rather good; no signs of rickets. Skin greyish and cool; fontanelle normal; no gaping sutures. Ears and fauces normal; stethoscopic examination normal; glands in the neck only just of the size of a pea. Abdomen normal; liver and spleen not palpable. Pupils equal, active to light; no strabismus, sometimes pronounced nystagmus. No difficulty in swallowing. The nape of the neck was drawn backwards. Kyphosis of the spinal column in the dorsal region. Hands firmly clenched and only extended with difficulty. Arms reflexly bent at the elbow and resist extension. The legs are kept adducted at the hip-joint, stiffly extended at the knees, the right leg hyperextended at the knee and not flexible, whereas the left leg yields to flexion, though after great

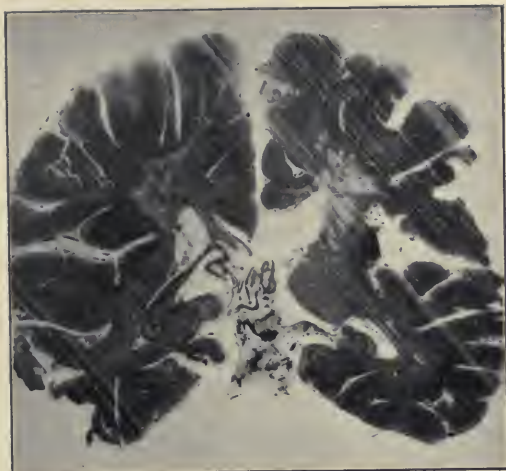


Fig. 8.

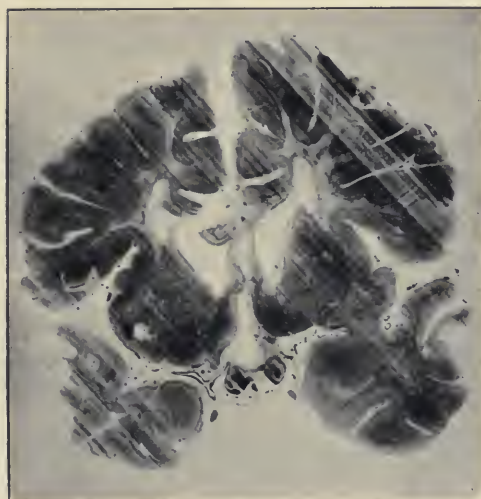


Fig. 9.



Fig. 10.

FIGS. 8 to 10.—Sections from the brain of Case 4, Gudrun A. B. Staining of Weigert-Kulschitzky-Wolters. For explanation of the figures see fig. 3, p. 79.

resistance. The feet are slightly in the equinus posture; they are not cold or œdematous. Patellar reflexes not obtained, no clonus of the foot. Periodic attacks of strong tonic rigidity, followed by screaming. Lumbar puncture on June 30; no fluid obtained.

The course of the illness during the six months' stay at the hospital was as follows:—

Temperature being at first normal, rose after a few days.

The stools at first were rather thin and gritty; later on they became normal, and remained so (July 3, 17 and 18 excepted). On September 17 the child began to get thinner. Vomiting occurred frequently once or twice daily; sometimes, however, the food was simply returned. The weight at first was increased from 5,050 gm. to 5,200 gm., then it fell rather evenly to 4,300 gm., and during the following months kept oscillating between 4,450 gm. and 4,300 gm. Finally it dropped to 4,000 gm. The urine was never found to contain albumen or sugar. In the beginning the patient was fed on milk and milk-pottage; later, on infants' food and barley water.

The following notes as to further course of the disease were taken from the ward journal:—

May 28: Condition not improved. Lies dozing most of the day; the spastic stiffness does not even cease during the sleep.

June 17: Ophthalmoscopic examination (Dr. V. Hertz) shows small equal pupils, active to light. As a rule, spasms of the downward movements. Under homatropine the discs were found to be bluish (probably physiological). The nasal edges were blurred, the veins strongly congested.

July 10: Mostly dozing, only cries when touched; no convulsions; nystagmus; no appetite; losing considerably in weight; no change of posture. Spastic hyperextended lower extremities, the head drawn backwards, and the back bent in the dorsal region; the hands clenched. Pupils equal; active to light.

July 25: Not able to swallow; nearly always dozing; purulent catarrh; lips dry.

August 31: Ophthalmoscopic examination: Pupils as before small, equal, active to light. Discs pale, especially in the left eye, veins prominent, nasal half more normal than before.

September 5: Nystagmus less pronounced than before. The spastic hyperextension of the lower extremities is unchanged. Upper limbs flexed at the elbows, hands clenched, stiffness of the neck, and curving of columna in the dorsal region. Fontanelle not distended, sutures firm. Circumference of the head, 43 cm.; circumference of chest, 37 cm.

September 28: Died at 11.30 p.m.

Autopsy fifteen hours after death showed abundance of serous fluid in the subdural cavity. Dura in some places adherent to pia; scattered smaller hæmorrhages. Pia not clear, somewhat œdematous. The lateral ventricles normal. The brain apparently rather diminished in size, but of normal shape. Consistence hard, almost cartilaginous. The cerebellum was in the same

condition. On the cut surface the glia tissue appeared to be increased. No further abnormality to naked-eye examination.

The posterior and basal portions of both lungs showed early infiltration. The mucous membrane of colon was swollen; the follicles stood out distinctly. Ductus Botalli closed.

Among the five cases described above, two (Cases 1 and 2) resembled one another so closely, both from the clinical and pathological aspect, that they obviously belonged to the same group. Case 4 must also be added to this group from the anatomo-pathological aspect, and, according to the rather imperfect description, from a clinical point of view as well. In Case 5, no microscopical examination was carried out, but the clinical picture, the naked-eye appearances and the consistence of the brain, entitle us to refer this case, too, to the same group.

With regard to Case 3 it may be maintained that—(1) the clinical picture bears a close resemblance to that found in the other cases (stiffness, spasms, &c.); and (2) it revealed the same macroscopical changes as those mentioned above, at any rate as far as the cerebellum was concerned. In considering the fact that in this case the rigidity remained unchanged till death, and that a severe dyspepsia was present, the most natural conclusion will be to rank this case along with the four others; this patient seems to have suffered from the same disease as the others, but owing to the gastro-intestinal complications died in an earlier stage, before the brain was fully sclerosed.

SUMMARY OF THE CLINICAL FINDINGS OF THE CASES.

The clinical picture of the above cases is very characteristic, but I should not dare to use it as the only point of support for diagnosis.

The first peculiarity about these cases—the family occurrence—will be discussed later on.

A characteristic feature of all the five cases is their acute onset at the age of 4 to 6 months in children who up to then had always been quite healthy. Only in one case (Case 2) was the child said to have been extraordinarily stiff all the time; it is, however, questionable how much stress may be laid upon this statement of the parents. As prodromal symptoms of the disease, causeless fits of crying and screaming were noted. Among the typical symptoms is the universal rigidity of the musculature of the body and the limbs, most pronounced in the lower extremities. A further stage of this rigidity is shown by the universal tonic spasms, which appear to be evoked by such stimuli as noise, light, or touching.

During the attacks the patients generally show the following posture: the head bent backwards, the back curved in opisthotonos; in Case 3, however, only the lumbar region was in lordosis, strong kyphosis being present in the dorsal region. The upper extremities are flexed at the elbow-joint, the hands in some cases clenched, in other cases placed in the obstetrical posture. The lower extremities are extended at the hip-, knee-, and ankle-joints, often adduced until they cross. As far as the cranial muscles are concerned, the spastic attacks were less pronounced. In two cases strabismus convergens was observed from birth and throughout the course of the illness; it did not, however, seem to increase during the attacks. In Case 5, on the other hand, no squinting was noted. In all cases nystagmus occurred, especially during the fits, and did not decrease till towards the end of the illness.

More difficult to settle is the question whether or not the muscles of the face were influenced by the spasms, as during the fits the patients cried and screamed violently. To the observer this conveyed the impression that the cries were a real reaction to the pain caused by the fits. The frequent occurrence of yawning in Case 3 may possibly be regarded as a spastic phenomenon of similar origin. The difficulty in swallowing occurring towards the end is rather a paralytic than a spastic phenomenon.

In addition to these attacks of tonic spasms, which seemed to be a higher stage of the permanent rigidity, regular eclamptic attacks, accompanied by strong clonic convulsions, were noted in several cases, although not very frequently. True paretic symptoms did not manifest themselves till towards the end of the disease, when the spastic condition gradually passed into a relaxed paralytic state. In Case 3, however, the rigidity remained till death.

It was impossible to make any observations on the sensory side. In Cases 2 and 3 there was at first reaction to pain, and in all cases reaction to all such pains as accompanied the convulsions. The presence of ataxia could not be determined, as the movements were at first so intensely spastic and then paretic that the patients were able to catch things (except in Case 1).

With regard to the sense organs, hearing seems to have been unaffected at first, as the patients were very sensitive to sound. In Case 2 this reaction was lost at the end. Sight, so far as Case 1 is concerned, was present for a few months, the patient being able to follow things with her eyes. The ophthalmoscopic results were, as a rule, characteristic; in three cases (1, 2, and 5) optic nerve atrophy

was observed, in Case 5 neuritis. In Case 4 no ophthalmoscopic examination was performed, and in Case 3 it gave a normal result. This, as already mentioned, may be due to the fact that the patient died before the affection had reached the same advanced stage as in the other four cases. The optic atrophy, therefore, seems to us to be a characteristic symptom, at any rate in the latest stages of the disease, and probably a sign of great diagnostic significance. The pupils in all cases were active to light, even in the latest stages (?). In Case 2 only was the reaction sluggish, and later on almost extinguished. The tendon reflexes of the upper extremities only are mentioned in Case 1 and described as brisk, whereas in none of the cases could the patellar reflexes be evoked, probably on account of the rigidity. As to the plantar reflexes, nothing can be judged from the notes at hand.

Restlessness and screaming were the chief symptoms in the beginning, succeeded by dulness. The mental faculties did not develop after the disease had begun. As a last sign pointing to the conditions of the central nervous system, the fontanelle presented a characteristic want of distension, and it was generally distinctly sunken.

In the periodic elevations of temperature (fig. 11) we find a symptom, the significance of which is not easy to interpret. In Case 3 the permanently elevated temperature probably must be ascribed to the dyspepsia, but in all the other cases no affection was found of the digestive tract, of the lungs, or of the urinary system, to which the short febrile periods might have been referred. In fact, they may be due to some occult infection or intoxication, and thus be regarded as a merely accidental complication. But, on the other hand, they may represent a characteristic feature of the disease, and thus be due either to an influence acting upon the temperature-regulating system or to the fact that the destruction of nervous substance, being the fundamental process of the disease, takes place at intervals, and causes elevation of temperature due to products of its destruction. It is, however, a matter of difficulty to judge from the ward journals as to the cerebral symptoms during febrile periods. According to the statement of Dr. Bloch, these periods were followed by aggravated cerebral symptoms; in Case 4 the convulsions and the screaming were far more pronounced during the duration of the elevated temperature, and in Cases 1, 2, and 3 this also seems to appear from the notes.

Great lowering of temperature was succeeded by coldness, debility, even by collapse and sometimes by eclamptic fits (Case 1). In Case 3, however, eclampsia also occurred outside the periods of subnormal

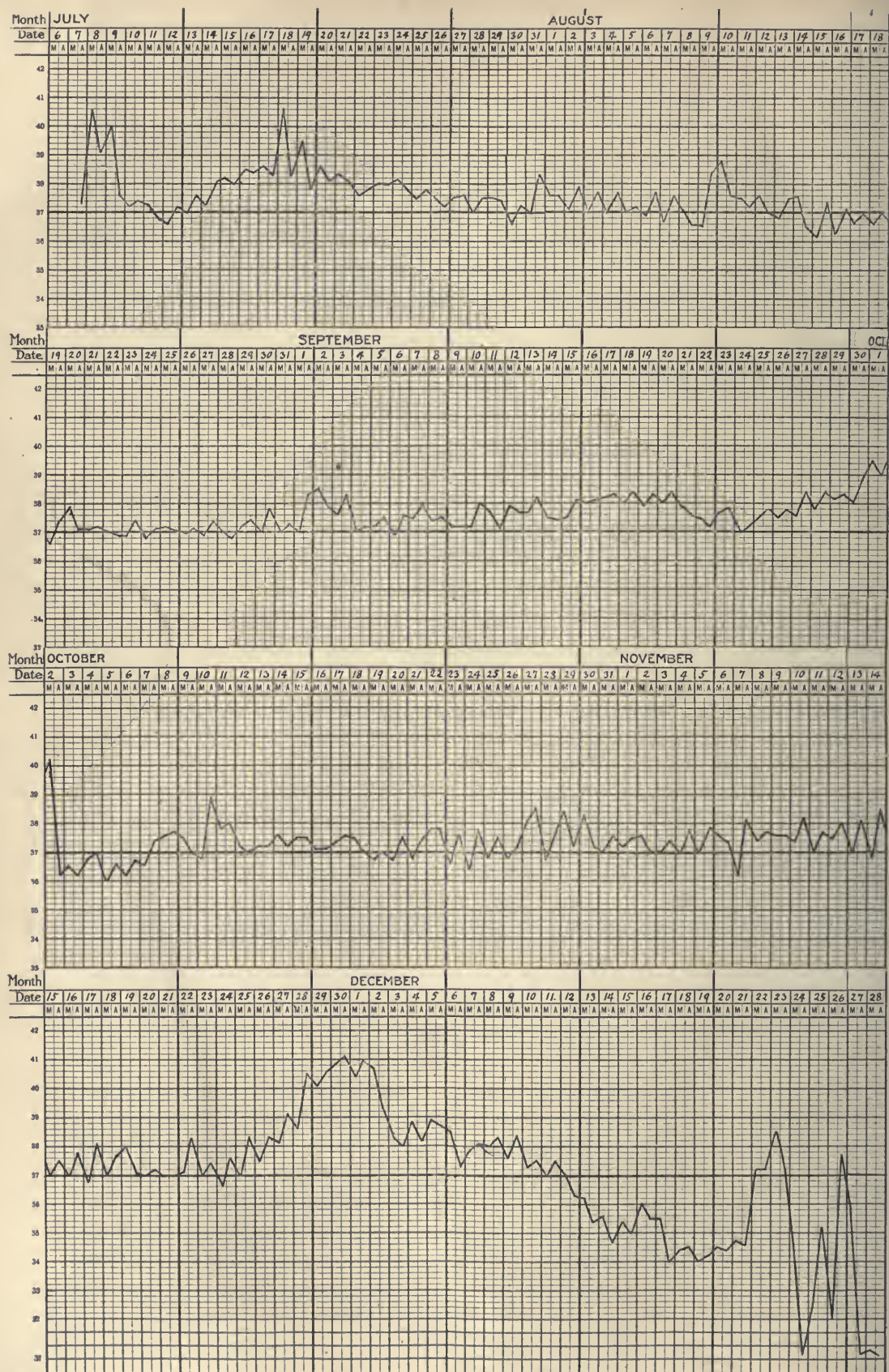


FIG. 11.—Temperature of Case 1 (Kai Bn.).

temperature. All the cerebral symptoms, the vomiting excepted, can be regarded as more or less casual complications. The vomiting was of rather frequent occurrence in the four last patients, but did not appear in Case 1, in which only slight regurgitation was noted. Diarrhoea occurred in Cases 1 and 5 a few times, in Case 2 not at all, but in Case 3 was almost permanently present, the stools being of a thin and mucous consistence. Here the dyspepsia probably had given rise to the albuminuria (the oedema), the stomatitis, the pharyngitis, the catarrh, the eczema and the conjunctivitis; some transitory catarrh and conjunctivitis in Case 5 and some pyuria in Case 1 excepted, no such severe complications were found in the other cases.

No affection of the heart nor the lungs occurred except the terminal pneumonia. The weight as a rule oscillated, decreasing during the latter period. The terminal increase of weight in Case 3 was due most probably to retention of urine.

It may be added that lumbar puncture and Wassermann's reaction, performed in two cases, gave negative results.

ANATOMO-PATHOLOGICAL CONSIDERATIONS OF THE CASES.

The most characteristic feature of the above cases, as far as their pathological anatomy is concerned, is the complete destruction of the axis-cylinders and medullary sheaths, the replacement of the destroyed tissue by neuroglia and the relative intactness of the nerve-cells. The destruction shows a peculiar distribution, as may be seen from the description of Cases 1, 2 and 4; the processes of all the nerve-cells of cortex cerebri and cerebelli are most affected; destruction of the processes from the basal ganglia represents the next stage and of those from the spinal centres the last stage of the disease.

This affection probably proceeds evenly, as, had it been of sudden occurrence, cysts and irregularity of the glia proliferation would have been present. The regular distribution of glia tissue without any deformation of the brain is most naturally explained by the steady substitution of glia in places where the nervous tissue was destroyed.

Furthermore the process must be looked upon as being no longer progressive in Case 1, and as nearly ended in Cases 2 and 4, on account of the extraordinarily scanty Marchi degeneration in the first case, and from the small number of fatty and of albuminous granules in the scavenger cells. To reconstruct the onset of the process from the existing pathological changes is, however, rather difficult, although it may be possible to draw some conclusions as to certain facts. The question is,

whether the affection is to be regarded as—(1) a variety of tumour-growth, (2) a repaired inflammatory process, or as (3) a simple degeneration of the nerve-cell processes.

The first explanation, that it is a kind of gliomatous formation, is entirely untenable. It is quite impossible that a tumour could occupy nearly all the white matter of the central nervous system, and abruptly terminate where it approached the grey matter, causing no deformation of the brain.

The explanation that it is due to an inflammatory process appears to be more probable, provided that we allow that when the presumed inflammation has passed away no infiltration with plasma cells, lymphocytes, or polynuclear leucocytes is traceable anywhere. In my opinion, the strict limitation of the lesions to the white matter seems to speak against an inflammation. Another objection to the theory of an inflammation in these cases is the peculiar distribution of the changes within the white matter. There is no distinctly marked focus, but a selective destruction which predominantly affects the processes of the cortical pyramidal cells, leaving the adjacent regions of the white matter, as, for instance, the tracts of pons, undamaged.

A third point of significance seems to me to be a comparison of the above cases with the one previously described by me under the name of "perivascular necrosis of the medullary substance." As was already emphasized in the previous paper, the changes—(1) were only found in the medullary substance, and not in the grey matter; and (2) consisted of a slight diffuse destruction of the medullary sheaths throughout the white matter and of a complete disintegration of the vessel sheaths. Corresponding with this was found—(3) a protoplasmic and partly fibrillary glia and great quantities of fatty granule-cells round the vessels, carrying away the decayed myelin sheaths.

This picture, in fact, corresponds exactly with the initial stage of the above cases of diffuse sclerosis. The age of the child being nearly the same, and other points of resemblance being present in the clinical history, I feel myself entitled to consider this case as an initial stage of those described in this paper, but a stage which was interrupted by death owing to gastro-enteritis.

If I am right in maintaining this assertion, it must also be supposed that the disease is not of inflammatory origin, as in the said case neither leucocytes nor lymphocytes nor plasma cells were found anywhere.

I am compelled, therefore, to refer the disease to a mere degenera-

tive process. I feel, however, inclined to alter my conception regarding the case previously reported. The fact that the destruction of the medullary sheaths was predominantly round the blood-vessels, and of a more scanty occurrence towards the periphery, was indicative of a perivascular origin of the process, and the slighter disintegration in the outer regions I referred to a secondary degeneration of such medullary sheaths as pass near the vessels.

This, however, might also be explained in the following way: the degeneration of the medullary sheaths sets in diffusely, and the more intense destruction round the vessels is due to the fact that the glia-cells, receptors of the products of destruction from the degenerated sheaths throughout the white matter, wander into the vessels and push aside the surrounding sheaths.

Which of these explanations may be acknowledged as the right one is difficult to decide. In the case here described the density of the fibrillar glia was more pronounced round the vessels than at some distance from them. But this dense glia only appears as a comparatively thin and sharply limited tube round some of the blood-vessels. The explanation might therefore just as well be based upon the supposition that the glia becomes particularly dense in places where the protoplasmic glia-cell wanders, carrying with it the products of destruction.

We are thus, on the whole, more inclined to believe that the perivascular destruction of the medullary sheaths and heaping up of glia-cells is not the primary but the secondary factor and the natural consequence of the diffuse destruction of the medullary sheaths and axis-cylinders. No final decision can be reached until a case has been examined which is more advanced than my first case.

In this place I might mention a case to which my attention was not drawn till after the completion of my first paper; this case was reported by Lewandowsky and Stadelmann, and a *post-mortem* examination showed a recent affection of the brain. The most characteristic feature was a heaping-up of glia-cells distributed in spots, but with no inflammatory symptoms, and the axis-cylinder processes were not preserved in places where the medullary sheaths were destroyed, as is the case in disseminated sclerosis. The patient in this case being an adult, I must, however, in spite of the parallel, look upon it as different from my own.

I have now come to the third possibility, which to my view is the most probable, namely, that the affection is a merely degenerative process, analogous to such degenerations as are frequently found in certain hereditary or familial nervous affections, as, for instance,

Friedreich's disease. This interpretation is not only based upon the advanced destruction of the medullary sheaths and of the axis-cylinders traceable without any signs of inflammation, but it chiefly rests upon the characteristic distribution of the degenerative processes. These, to a certain extent, are just as selective as the degenerations in the hereditary nervous diseases; the tracts destroyed consist of all the axis-cylinders of the pyramidal cells of the cortex cerebri and the cells of the cortex cerebelli, together with their medullary sheaths. Corresponding with this, the degenerations met with in the central part of the brain and in the spinal cord mostly affect the pyramidal and cerebellar tracts, whereas the spinal nerve tracts are relatively intact, and the nerve processes from the centres of the spinal cord are all but undamaged.

I therefore believe that the degeneration of this enormous amount of nerve tissue is the primary factor of the disease, whereas the glia proliferation and the infiltration of the medullary sheaths with the gliogenous fatty granule-cells and other scavenger cells represents a secondary process.

EXPLANATION OF FIGURES.

Figs. 12 to 16 are stained with Alzheimer's acid-fuchsin.

Fig. 16 with Alzheimer's staining with Mallory's hæmatoxylin. The background fibres are neuroglial fibres. All the sections are from Case 1, Kai Bn. The figures are drawn by the author with a Zeiss's microscope, ocular ii, objective immersion $\frac{1}{1\frac{1}{2}}$.

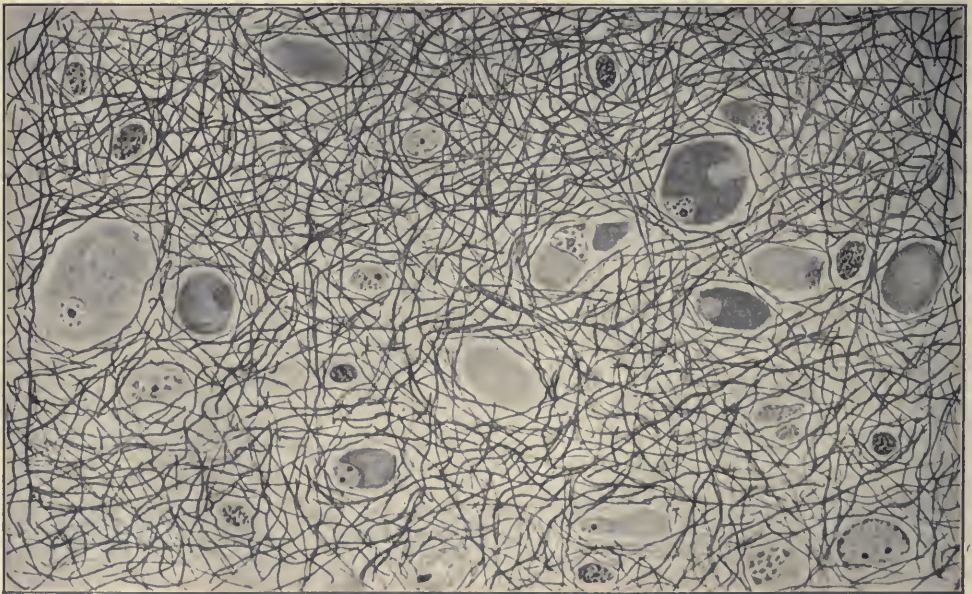


FIG. 12.—White substance of the hemispheres. The whole white substance is replaced by neuroglia in which may be seen many different types of neuroglial cells, small and large.

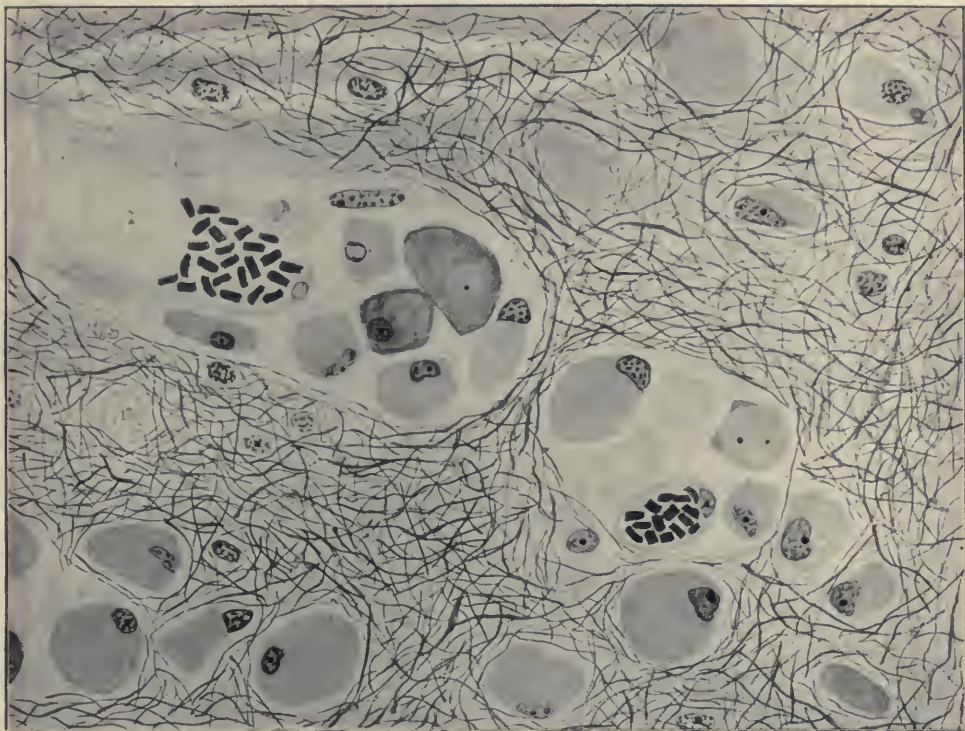


FIG. 13.—White substance of the hemispheres replaced with neuroglia. Two vessels can be seen (the erythrocytes are stained red) surrounded with gliogenous “scavenger” cells.



FIG. 14.—Grey substance of the hemispheres. The nerve-cells seem normal, and there is no augmentation of the neuroglia; only one neuroglia cell with fibres is seen.



FIG. 15.—Partly from the internal capsule; the white substance is replaced by abnormal neuroglia, gigantic polynuclear glia-cells with big fibres and degenerated nuclei.

THE NOSOLOGICAL PLACE OF THE DISEASE.

The above five patients, and probably the one previously described by me, present so many points of resemblance from a clinical and especially from an anatomo-pathological point of view, that it can scarcely be doubted they belong together. The most conspicuous feature, as far as their pathological anatomy is concerned, is the extraordinary hardness of the white matter of the brain and the spinal cord.

Several cases have been reported in the literature under the name of diffuse sclerosis of the brain, in which the main characteristic has been just such hardness of the brain. In fact, no other cerebral affection presents a similar hardness, and I thus feel entitled to classify my cases temporarily in one disease-group.

On the other hand, it may be considered beyond doubt that such sclerosis of the brain in most cases represents the final stage of various processes which are pathogenetically different, and previous authors

have tried to discriminate special forms within the category of diffuse sclerosis of the brain. One of the most prominent papers on this subject is written by Schilder. He not only gave a detailed report of the clinical and pathological findings of his own case, but also instituted a re-examination of the literature, and called attention to the cases



FIG. 16.—White substance of the hemispheres replaced with neuroglia. Shows the spider-cell forms.

already described as diffuse sclerosis of the brain; he gathered together such cases as have been published under other names, but which should be referred to this group. He thus separates four cases as a special group under the name of encephalitis periaxialis diffusa, considering them to be related to the disseminated sclerosis.

My cases, however, present certain peculiarities in which they differ considerably from the cases described by Schilder; thus they began in babyhood, they tended to occur in families, and they showed a complete absence of any signs of primary or secondary inflammatory processes. In the literature I have found one case—viz., Beneke's—which may be classified with the cases reported in the present paper.

Finally, there are certain cases reported in literature of syphilitic origin; but no syphilitic origin existed in Schilder's case or in my cases, and these syphilitic cases fall into a group by themselves.

In the following pages I shall discuss these three groups, giving, however, but a brief summary of the first and second group, whereas of the third a more detailed report will be given. I only refer to the disease in children.

Group I: the syphilitic.—It is no easy task to draw the line between syphilitic and the non-syphilitic cases. Some of the cases of the next group are probably syphilitic in origin, such cases, for instance, as are antecedent to the Wassermann reaction and where syphilis was present without being noted in the history. On the other hand, cases in which Wassermann's test proved positive, or cases in which syphilis was discovered in the history, might be ascribed to casual complications. Considering the varying forms under which syphilis generally appears in the central nervous system, I should, however, think it the most natural solution to explain these cases as syphilitic.

The first group, then, comprises the following cases:—

Buss: Hereditary syphilis in a child aged 2 years 6 months. Strümpell's case, in which the father suffered from typical tabes dorsalis. Haberfeld and Spieler's second case, in which the mother was syphilitic; and finally the case, reported and illustrated by Zappert, in the chapter on the central nervous system in the "Text-book of Pfaundler and Schlossmann," and a case observed by Pfaundler, in which syphilis was present, consanguinity of the parents, and paralysis of the father. Although the evidence of syphilis in these cases is not always to be relied upon, the disease must still be referred to a syphilitic affection, and the more so as *post-mortem* examination in several cases showed no particular limitation to the white matter, but an extension to the grey matter, combined with grave changes in the ganglion system, or with chronic meningitis. The case described by Bullard may also be placed among the syphilitic affections, which, although no history of syphilis was present, microscopically resembled general paralysis.

Group II: encephalitis periaxialis diffusa.—The second group comprises cases for which Schilder has proposed the name of encephalitis periaxialis diffusa, and which are in his opinion related to disseminated sclerosis. As to the relationship I shall not express myself any further, Schilder having thoroughly discussed the reasons for and against. On the whole, we may agree with the conception that some cases of diffuse sclerosis of the brain are especially extensive disseminated sclerosis. Schilder himself places in this group, in addition to his own case, the cases reported by Rossolimo, Ceri, Habermeld-Spieler and Beneke. For reasons which will be discussed later on, I should, however, feel inclined to refer the last case to the next group. There are, moreover, a number of cases which may well belong to this group, in spite of the pathological-anatomical description not being always detailed enough to permit any sure definition of the disease. This, for instance, applies to the cases reported by Schüle, Longkamp (first case) and Meine. A copious description of the chief characteristics of these cases having been already given by Schilder, I shall only here refer to his paper.

Group III: the familial early infantile form of diffuse brain sclerosis.—Regarding the pathogenesis of our cases and their place within the nosology, it may at first be noticed that they are absolutely different from the syphilitic group; there was no clinical evidence of congenital syphilis, and the pathological-anatomical findings differed from those found in syphilitic lesions. My cases differed, moreover, fundamentally from Schilder's encephalitis periaxialis diffusa. This affection, as a rule, seems to be indicative of a reparative inflammation, and the process does not affect the whole central nervous system; but as far as the cerebrum is concerned it appears to be confined to certain regions. The disease sets in during later infancy, and is of no familial occurrence. Against the latter assertion, however, Halberfeld and Spieler's case may be quoted, in which a relative of the patient was said to have been subject to the same disease. Let it be remembered, though, that this statement was due to the parents and not to the physician, for which reason the family occurrence may be regarded as somewhat doubtful. The process in my cases has been degenerative and not inflammatory, and affected the whole cerebrum and cerebellum; it always began during the first six months of life, and in four out of five cases presented a familial occurrence.

All these conditions point away from encephalitis periaxialis diffusa, and are totally unlike any form of disseminated sclerosis. Furthermore,

disseminated sclerosis is very rarely of familial occurrence; in fact, authors such as Müller will not acknowledge cases of familial appearance as disseminated sclerosis. Finally this disease is very seldom found in children; among fourteen cases reported by F. Wolf (1912), only one (the author's own case) could be traced back to the first year of life, and this, too, must be considered very doubtful. At any rate, the diagnosis was not verified by autopsy.

The pathological-anatomical findings, however, and the familial occurrence point to another group of diseases—namely, the hereditary familial nervous affections. The isolated occurrence in Case 5 is of but small importance, firstly because all familial diseases may appear sporadically, and secondly because the case, on the whole, is in perfect keeping with the other cases as far as the clinical and pathological findings are concerned.

It is equally evident that there is just as deep a separation between my cases and Schilder's encephalitis periaxialis diffusa as between Friedreich's disease and disseminated sclerosis.

In attempting to place my cases of hereditary familial nervous affection, the point is, to which of these groups are they most intimately related? The two groups of disease to which my cases may belong are, on the one hand, Pelizaeus-Merzbacher's disease, aplasia axialis extracorticalis congenita, and on the other, Tay-Sachs' type of familial amaurotic idiocy.

My cases resemble aplasia axialis extracorticalis congenita in that they set in during the first years of life, and show pronounced destruction of the white matter of the brain. But there is a considerable difference in the clinical picture and in the course of disease. Aplasia develops to a certain point and then remains stationary. In my cases the pathological process, on the contrary, advances inflexibly and relatively quickly until a fairly complete destruction of the white matter of the cerebrum is produced. In this respect my case presents a kind of the relationship to familial amaurotic idiocy. This, on the other hand, forms a supplemental contrast to my cases, the most characteristic feature being the degeneration of nerve-cells, whereas it is the destruction of the axis-cylinders and myelin gains which characterize my cases.

It is universally recognized that there has been a somewhat exaggerated tendency to divide the familial nervous and muscle diseases into a countless number of types representing only transitional forms. It seems to me, however, that my cases show pictures so typical and distinct from all other cases, even from Pelizaeus-Merzbacher's disease,

that I am entitled to regard them as a special group within the familial nervous diseases, and, in fact, a group to which the name of *familial early infantile brain sclerosis* may rightly be given.

The next question of interest is, which of the cases previously described in the literature ought to be referred to this group? The most minutely reported case is that of Beneke, but unfortunately it contains no clinical history, only a pathological-anatomical description.

Beneke's case was a boy aged 1 year 9 months, 51 cm. in length. *Post-mortem* examination showed a double-sided pneumonia, ecchymoses on the abdomen, and contraction of the elbow-joints, but otherwise no abnormality, except in the central nervous system. The pia was hyperæmic and œdematous. The shape of the brain did not show much change other than a great increase of consistence. This increase was also found in the basal ganglia, in the bulbus olfactorii and in the optic nerves. In the cerebrum itself there was no sclerosis of the cortex, but only of the white matter and, to a certain extent, of the basal ganglia and the central nuclei, such as the nucleus caudatus, claustrum, &c. In the cerebellum an extensive sclerosis was noted coincident with a soft focus in the cortex. There was no encephalomalacia. The spinal cord was also intensely sclerosed. The sclerosis did not seem to be total as in my cases—it consisted of large confluent foci intermingled with traces of white matter. As in my cases, a narrow streak of white substance, fairly undamaged, was found immediately under the cortex. The occipital lobes and the frontal lobes presented the softest consistence. When examined under the microscope the tissue was found to show a copious increase of glia corresponding to the grey foci. The cell types showed all transitional stages from glia cells without a protoplasm to large polymorphonuclear homogeneous cells with a peripheral arrangement of the nuclei. The latter forms were generally found in dense layers round the larger or smaller blood-vessels, or formed isolated punctiform groups in the middle of the glia tissue. The substance between the cells was hard, fine and densely fibrillated. Within the dense sclerotic regions, medullated nerve-fibres were found which had escaped destruction, mostly arranged peripherally. Everywhere fatty granule-cells were noted, but not in very great quantities. In contradistinction to this, the sclerosis of the spinal cord chiefly consisted of dense masses of glia-fibres without any special increase of the glia-cells. The fatty granule-cells were quite wanting here and some of the ganglion-cells were degenerated. The process seemed to be progressive in the brain, and finished in the spinal cord.

The author calls attention to the difficulty of proving whether the process might be an inflammation, a congenital anomaly of growth, or a kind of tumour formation; the analogous large cells can be found in many gliomata, and also in regenerative processes.

Beneke's report seems to correspond with my cases in all essentials, the only difference being that the process was not so advanced here as in my cases. The child is presumed to have died during the development of the affection.

Among other reported cases from early infancy two only can be referred to this group—namely, the cases reported by Schmaus and by Heubner. In both cases, however, the patients were somewhat older children (Heubner's, aged 5; Schmaus's, aged 3). The pathological-anatomical findings do not permit me to classify them with certainty. It may be added that in none of these three cases were other members of the family affected.

As will be evident from this review of the literature, not many cases are recorded in early infancy, and it therefore appears remarkable that Zappert, in "Pfaundler Schlossmann's Text-book," states that the disease is of frequent occurrence in small children. ("Vorwiegend werden von der diffusen Sklerose Kinder in den ersten Lebensjahren selten grössers Kinder, oder Erwachsene betroffen.")

Nearly all his references to literature apply to adults or to older children.

SUMMARY AND CONCLUSIONS.

(1) The so-called diffuse sclerosis of the brain in children may be divided into at least three quite distinct types: (i) A syphilitic form; (ii) Schilder's encephalitis periaxialis diffusa; (iii) a familial infantile form, of which five cases are discussed in the present paper; the literature probably contains one other case.

(2) This form shows the following characteristics: it is usually a familial disease; it sets in somewhat acutely in about the fifth month in a child who up to then has been quite healthy; it progresses on a chronic course, ending with death, five to six months after the onset; universal rigidity of the musculature, violent tonic spasms, probably causing pain, and brought on by touching or noise form characteristic symptoms. As a rule, nystagmus is present, and in the latter stages atrophy of the optic nerve. Periodic elevations of temperature occur without perceptible cause, outside the central nervous system. Finally, extensive paresis and pronounced debility close the scene.

(3) The pathological-anatomical findings are: a marked hardness of the white substance of the brain without alteration of its shape. Microscopical examination of three cases showed relative intactness of cortex and the basal ganglia, the nervous centres of the brain and of the spinal cord; destruction of the medullary sheaths and axis cylinders throughout the white substance of the cerebrum (a 2-mm. layer, however, is preserved immediately under the cortex). Complete destruction of the white matter of the cerebellum and degeneration of the spinal nerve tracts are present. The destroyed tissue is replaced by dense fibrillar glia, in which are seen a considerable number of variously shaped glia-cells, mostly protoplasmic; the vessel sheaths are infiltrated with fatty granule-cells and other apparently gliogenous scavenger cells. There is a total want of new formation of vessels or infiltration of the vessel sheaths with plasma-cells, lymphocytes, or leucocytes.

(4) The affection must be regarded as a purely degenerative and not as an inflammatory process. The disease presents a certain relationship to Pelizaeus-Merzbacher's disease, aplasia axialis extracorticalis congenita, on one side, and to Tay-Sachs' form of familial amaurotic idiocy on the other side. In other respects, however, it differs conspicuously from both these groups.

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ACUTE POLIOMYELITIS.¹

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¹ The Lumleian Lectures, for 1916, delivered before the Royal College of Physicians of London.

CHAPTER I.—INTRODUCTION.

MR. PRESIDENT AND FELLOWS,—I would in the first place wish to thank the College for the honour they have conferred on me by their invitation to deliver the Lumleian Lectures for 1916.

The subject, acute poliomyelitis, is one which has not previously been dealt with by a Lumleian Lecturer, although a consideration of some points formed part of Farquhar Buzzard's Goulstonian Lectures, delivered in 1907. [33].

Since that date not only has poliomyelitis spread in epidemic form over the face of the globe, but considerable advances have been made in our knowledge of the disease. It is true that previous to 1905 small epidemics had occurred, but it is only since that date that it has had its present wide prevalence.

During the last six years the experimental investigation of Flexner and his co-workers at the Rockefeller Institute, of Levaditi at the Pasteur Institute, and Leiner and von Wiesner in Austria, and Römer in Marburg, have thrown much light on the nature of the disease.

A wider knowledge of the clinical manifestations has been gained, and the investigation of acute cases has rendered the pathological process more clear.

It is my purpose to put before you in these Lumleian Lectures the epidemiological, experimental, and clinical observations, and some points with regard to treatment of the acute stage of the disease.

It is during the last five years that poliomyelitis has been recognized by the Public Health authorities in England as a definite specific fever, and notification has been adopted. The British Islands have suffered comparatively little during the epidemic period.

Although much has been discovered with regard to its nature, it has not yet been possible to apply that knowledge to its prevention, and much investigation still remains to be done, not only in the experimental, but also in the clinical and epidemiological fields.

The likeness which the disease bears to rabies has raised the hope that precautions, which have been so successful in dealing with that infection, might be able to control poliomyelitis, but in its spread it bears such a likeness to that of meningococcal meningitis that this can hardly be expected. It seems unlikely, however, that any effectual remedy, other than prevention, will be found for a disease which is so fulminating in attack and so destructive in its effects on the central nervous system.

The first lecture will be devoted to the epidemiology and pathology ; the second to the experimental side, and the third to the clinical consideration of the subject.

The names which have been used and suggested for the disease are numerous: spinal infantile paralysis, epidemic infantile paralysis, epidemic poliomyelitis, meningo-myelo-encephalitis disseminata, polio-encephalo-myelitis, Heine-Medinische Krankheit, acute anterior poliomyelitis, and acute poliomyelitis.

There is no doubt that the terms meningo-myelo-encephalitis disseminata and polio-encephalo-myelitis most accurately describe the anatomical and pathological changes; but the name "acute poliomyelitis" has now come into such general clinical use, and is used to describe the nature of the virus, that it is inadvisable to attempt to replace it. All that is required is that poliomyelitis shall be recognized as one of the acute specific fevers, having a tendency to affect any part of the central nervous system, and giving rise to a variety of symptoms dependent on the portion affected.

EPIDEMIOLOGY OF POLIOMYELITIS.

(1) *Historical.*

The history of the earlier epidemics of poliomyelitis has been written by Allen Starr [26], Holt and Bartlett [12], who collected the records of thirty-five epidemics of poliomyelitis up till 1907, and further details were reported in the papers of Wickman [27], Job and Froment [14], and Sever [25].

In 1911 I collected additional records of some twenty-six epidemics in all parts of the world, and these, together with those previous to 1907, are recorded in a paper on the subject published in *BRAIN* of that year [1].

(2) *World-spread.*

The leading features of the past epidemics may, however, be shortly stated. The first record of the disease in an epidemic form came from Sweden in 1881. In 1883 some groups of cases were recorded in Italy, and in 1886 in Norway, Germany, and France. All these epidemics were small in numbers. In 1887, Medin described an epidemic in Stockholm of forty-four cases, and this is the first important work on the subject. In 1894 an epidemic of 132 cases occurred in Rutland, Massachusetts, which was recorded by Caverly and McPhail. Small epidemics were recorded in the "nineties" in Italy, France, Australia,

England and America, and a larger one occurred in Vienna (forty-two cases) in 1898, and in Norway and Sweden in 1899. This last was described by Wickman, to whom so much is due in regard to the investigation of the pathology and the spread of the disease. In the middle of the next decade—viz., 1900 to 1910—the record of cases, which before had been limited to two figures, now reached to four figures, and during the years 1903-07 it may be said that the disease was pandemic in Norway and Sweden. During the years 1907-10 large epidemics occurred in the States of New York and of Massachusetts. At the same time epidemics of the disease were recorded in Australia (Stepheris), in Vienna (Zappert), Westphalia (Krause and Reckzek), in Paris (Netter), in Austria (Furnratt, Potpeschnigg, Lindner and Mally), Switzerland (Hagenback), and in Russia (Jogichess).

During the year 1910 the total number of cases and deaths from poliomyelitis in the United States was 5,093 and 825 respectively, a mortality of about 13.75 per cent. The epidemics in Massachusetts in 1909 and 1910 were most carefully investigated by Lovett [17] and his co-workers; and in Cincinnati and Batavia in 1911 and 1912 by Wade Frost [9], in regard to all the following factors: rainfall, temperature, surroundings, nearness to railroad, nearness to water, age of house, sanitary conditions, location of house, character of house, floor of house inhabited by a family, sewage disposal, character of water supply, relation to dust, prevalence of vermin, insects and rodents, data as to domestic animals kept, occurrence of paralysis in animals, swimming and wading, exposure to heat, cold or damp, diet, and attendance at school. No common factor could be found. No relation to dust, prevalence of vermin, or the keeping of domestic animals could be ascertained, and the same is true of the numerous other points investigated.

(3) *Factors common to all Epidemics of Poliomyelitis.*

There are, however, certain factors common to all epidemics, and these may be shortly stated.

Seasonal relationship.—In the Northern Hemisphere the disease always has the greatest prevalence during the months of July, August, September and October, the months of August and September being nearly always those in which the greatest number of cases occurs. In the Southern Hemisphere the disease has occurred during the months of March and April—i.e., months which, I believe, in atmospheric conditions correspond fairly well to September and October

in the Northern Hemisphere. The disease was supposed not to occur in the Tropics, but an epidemic was reported in Cuba in 1909 by Lebrede and Recio [16], the maximum number of cases occurring in July and August, and in the island of Nauru, in the Southern Pacific, in January, 1909, by Müller [20]. It is interesting in the latter epidemic to note that it affected the natives of the island very severely. In this island, which has a population of 1,250 natives and 1,000 imported labourers (partly Chinese and partly Caroline Islanders) and about 80 whites, there were 700 cases of the disease: of these 38 died; 470 of the 700 cases occurred in natives of the island, and of these 37 died. The Chinese were unaffected, and only three Europeans were attacked. So the disease fell with peculiar severity on the native population and the imported Caroline Islanders.

Age-incidence.—The incidence of the disease on young children is a constant feature, and it commonly attacks these during the second and third years of life. Babies in arms are rarely affected, and as the age advances the incidence rapidly declines.

Mortality.—The mortality in the various epidemics varies considerably; over the total number of cases it amounts to from 11 to 12 per cent. Of the notified cases in England during the years 1912-13-14, the mortality was 13 per cent., 14 per cent. and 16·6 per cent. respectively; but this hardly represents the true mortality, which is probably considerably lower, for it is certain that many of the milder and abortive cases are not notified.

Incubation.—In the Swedish epidemic of 1905 (Wickman) the incubation period was shown to lie between one and four days, seventy-four of the 127 cases coming within this period. Currie and Bramwell [8] brought forward some very good evidence from a small localized epidemic in Tillicoultry that it was four days or less. There are some striking individual cases of isolated contact which show that the incubation may be as short as twelve hours.

Spread of infection.—Wickman showed that the disease spread by means of carriers along the lines of communication—road, railways, &c. He brought forward evidence of the spread of infection from school. The school epidemic reported by Wickman occurred in Trästena, a little village of 102 houses, of which nineteen were affected. The school was infected by a child attending on June 28, and a series of cases which could directly or indirectly be traced to the school occurred on July 3, July 4, July 8, July 10, and July 12. The school was shut on July 15. Other cases occurred during the month, and the last on August 4.

In this little parish of Trästena, with 500 inhabitants, forty-nine persons were affected, twenty-three with the abortive form of the disease, twenty-six with the paralytic form. Of the cases with paralysis, eleven died—i.e., 42·3 per cent. Three other instances of a school being a source of infection are given by Wickman. The disease appears always to be carried by contact, but the “carrier” may be a perfectly sound and healthy individual. Further evidence on school infection was collected by myself in 1911, but although isolated cases of poliomyelitis occasionally occurred in schools in England, yet no evidence of spread from this source was forthcoming [2].

The disease rarely occurs or spreads in institutions. An investigation in America of forty-five institutions in which 3,600 children resided, showed that only one child contracted the disease during an epidemic period.

(4) *Poliomyelitis as an Epidemic Disease in Great Britain.*

So far as I know, there is no record of any epidemic of poliomyelitis in England before 1897, when W. Pasteur [21] described the affection in seven members of one family. That record has become historic, as it is the highest number of members affected in the same family.

Thomas Buzzard [6], in 1898, published a lecture “On Cases illustrating the Infective Origin of Infantile Paralysis.” He gives an instance of two sisters residing in the same house who were attacked with paralysis within six days of each other. Four other children of the same family escaped. Two other children living in a neighbouring street were taken ill in a similar way in the same week. He also mentions a case, seen in 1895, of a brother and sister who were taken ill within two days of one another; the sister was feverish and recovered without paralytic symptoms, the brother was paralysed in the left arm. These two cases are alluded to in Buzzard’s Presidential Address before the Clinical Society in 1895.

It has, of course, long been recognized that poliomyelitis is prevalent during the summer months in London, and especially during August and September. I recorded an undue prevalence in 1904.

In 1908 Treves reported an epidemic of eight cases at Upminster, a small village in Essex.

In 1909 an epidemic of thirty-seven cases was reported by George Parker in Bristol.

In 1910 Garrow reported cases of poliomyelitis in Cumberland, notably in Carlisle and Barrow-in-Furness.

Dr. Beard, the Medical Officer of Health in Carlisle, recognizing that the disease was occurring in an epidemic form, obtained the sanction of the Health Committee to make the disease notifiable.

NUMBER OF CASES OF POLIOMYELITIS IN ENGLAND AND WALES
FOR THE YEAR 1912.



FIG. 1.—The figures indicate the number of cases of poliomyelitis notified in each county during the year 1912.

This, I believe, was the first place in which notification was instituted in this country. In this year epidemics also occurred at Melton Mowbray, Cerne Abbas [1] and around Edinburgh [18].

In 1911 numerous epidemics were recorded throughout England; notably in Devon and Cornwall and in the Eastern Counties [4]. That in Devon and Cornwall was carefully investigated by Dr. Reece [23], the Inspector of the Local Government Board, but no definite conclusion was arrived at as to the mode of spread of the infection.

**NUMBER OF CASES OF POLIOMYELITIS IN ENGLAND AND WALES
FOR THE YEAR 1913.**



FIG. 2.—The figures indicate the number of cases of poliomyelitis notified in each county during the year 1913.

(5) *Distribution of Cases of Poliomyelitis in England for the Years 1912, 1913, 1914 and 1915.*

The study of the notified cases of poliomyelitis in England during the years 1912, 1913, 1914 and 1915 shows that the disease is distributed in a very irregular manner (figs. 1 to 4).

NUMBER OF CASES OF POLIOMYELITIS IN ENGLAND AND WALES
FOR THE YEAR 1914.



the same years is to be noted in the contiguous counties of Cheshire, Staffordshire and Warwickshire, and with the same sharp decline in 1915. Northamptonshire, Bedfordshire and Buckinghamshire, severely attacked in 1912, have remained fairly free since.

NUMBER OF CASES OF POLIOMYELITIS IN ENGLAND AND WALES
FOR THE YEAR 1915.



FIG. 4.—The figures indicate the number of cases of poliomyelitis notified in each county during the year 1915.

Gloucester had a high incidence in 1915, as had also East Sussex, neither of these counties being severely affected in the previous years. The study of these maps suggests that poliomyelitis is, in its

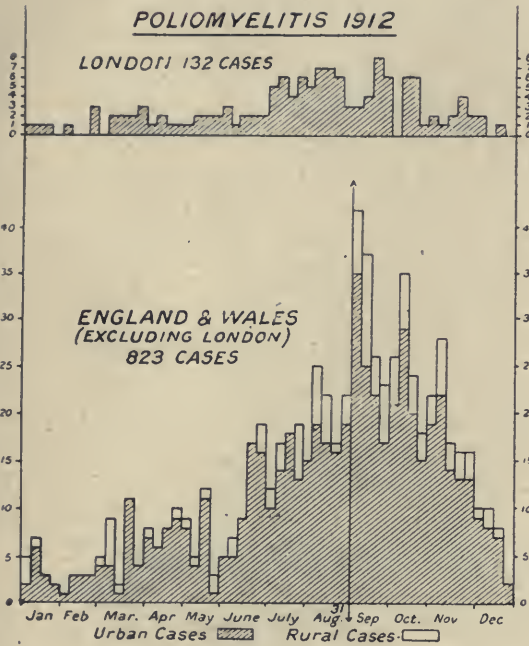


FIG. 5.

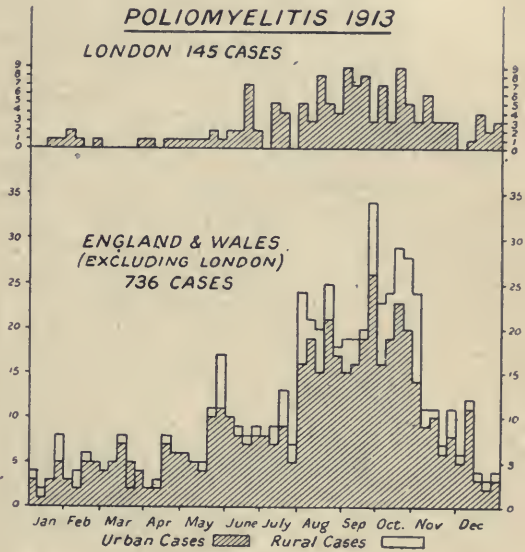


FIG. 6.

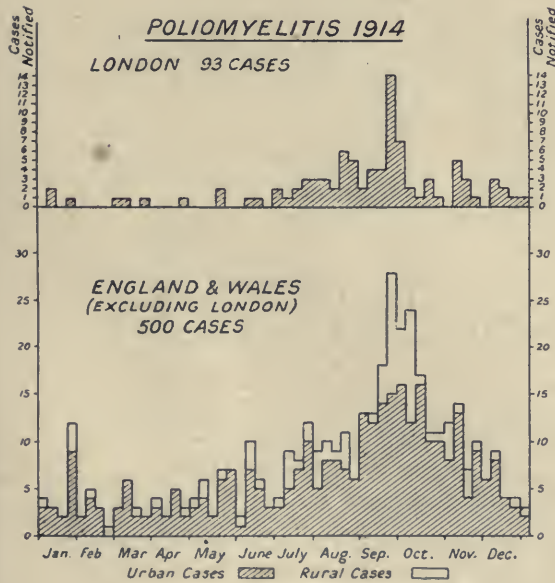


FIG. 7.

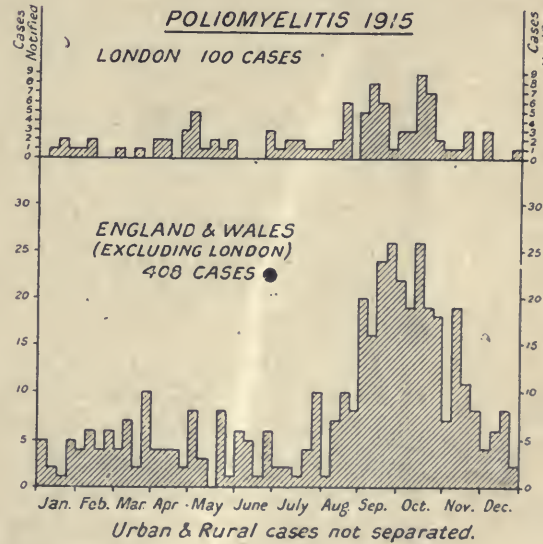


FIG. 8.

distribution, similar to meningococcal meningitis, only a very small percentage of the population being affected.

In September, 1911, the Local Government Board, on the recommendation of the College of Physicians, made the disease compulsorily notifiable for London, and in September, 1912, for the whole country.

For the years 1912-13-14-15 some idea can be obtained of the distribution throughout the community. This is indicated on the charts (figs. 5 to 8) kindly supplied to me by Dr. Reece, of the Local Government Board, and on the maps (figs. 1 to 4) compiled from the monthly returns.

During the year 1912, 823 cases of poliomyelitis were investigated by Dr. Reece, of the Local Government Board. The mortality for all ages was 13 per cent.; 51·9 per cent. recovered with permanent paralysis, so that the disease either killed or incapacitated to a greater or less degree 65 per cent. of those who were attacked, leaving a figure of 35 per cent. for complete recovery.

During the year 1913, 736 cases of poliomyelitis were investigated. The mortality for all ages was 14·4 per cent.; 53·6 per cent. recovered with permanent paralysis and 14·4 per cent. died. The disease thus killed or incapacitated in a greater or less degree 68 per cent. of those attacked. These figures would leave a figure of 32 per cent. for complete recovery.

During the year 1914, 500 cases of poliomyelitis were notified. The mortality for all ages was 16·6 per cent.; 47·7 per cent. recovered with permanent paralysis, so that the disease killed or incapacitated in this year to a greater or less degree 64 per cent., leaving a figure of 36 per cent. for complete recovery.

For the year 1915 complete figures are not available; it is known, however, that 408 cases were notified, and their distribution about England is shown in the map. The mortality and incapacity cannot be stated, but the figures for the three years 1912-13-14 having been 65, 68 and 64 respectively, it is unlikely that 1915 would show any great variation.

During the year 1913 an epidemic of poliomyelitis occurred in certain districts in Lancashire and Westmorland. Macewen [19], who investigated the epidemic, says: "It will be observed that the outbreak of poliomyelitis in Barrow was marked by its restriction to young children. The reason for this exceptional incidence of the disease on young children is one of the problems connected with poliomyelitis which still seem to need elucidation."

It is indeed a striking fact that of the nineteen cases specially investigated in Barrow, only two were over the age of 3 years, Nos. 1 and 16, aged 4 and 5 years respectively, occurring in groups 1 and 2 as indicated on the map (fig. 9). Now it is well known that Barrow suffered from a severe epidemic of poliomyelitis, investigated by

BARROW-IN-FURNESS.

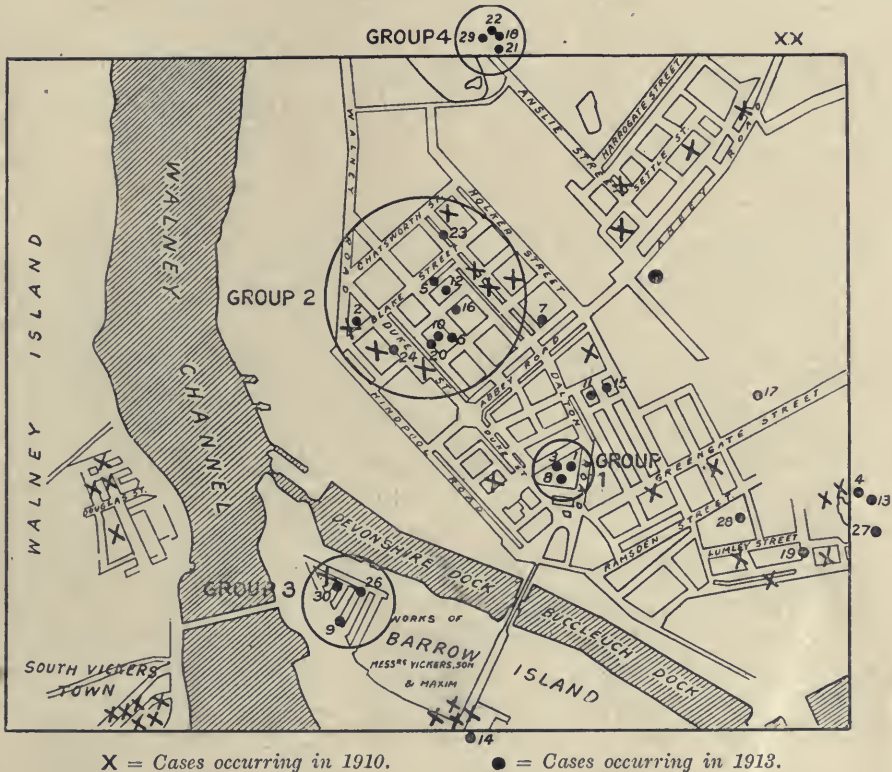


FIG. 9.—Map of Barrow-in-Furness: The x indicates the position of cases which occurred in 1910, investigated by Dr. Garrow; the • indicate the position of cases occurring in 1913; the numbers, the sequence of the date of onset of the disease; and the circles, groups into which they are arranged by Dr. Macewen.

Garrow [10], in 1910, which left some thirty-seven cripples. So the disease when it occurred again in 1913 fell upon a locality in which the susceptibles had been picked out by the former epidemic, and the population (except for those who had come into existence since 1910) were naturally immune, or had an acquired immunity. It would seem that the susceptible material of a population is fairly soon exhausted. The disease therefore fell on those below the age of 3 years.

It is of interest also to compare Macewen's spot map of the incidence of poliomyelitis in Barrow-in-Furness, 1913, with that of Garrow's in 1910, and notice that the largest group (No. 2) tends to fall into the same area as a considerable number of Garrow's cases. This may be dependent on certain local conditions or may be due to a "virus carrier."

It seems possible that the careful investigation of the various epidemics of this disease will bring to light some causative factor, but it is essential that such investigation should take place at the time of the occurrence of the acute disease and not when the after-effects are the sole record of the epidemic. So far it must be admitted that factor has not been found.

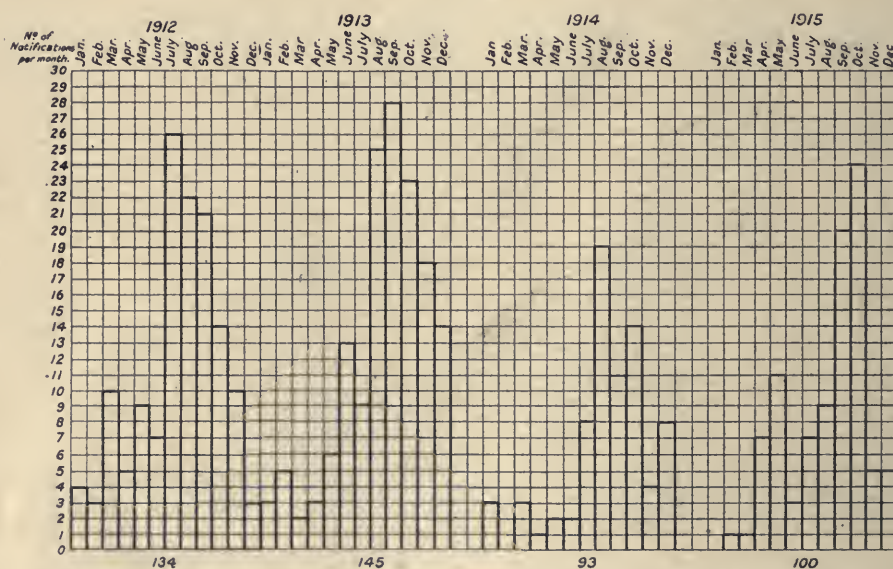


FIG. 10.—Chart showing the monthly returns of cases for years 1912-13-14-15 for the London area. It will be noted that in 1915 the maximum number of cases occurred during October, and not during August and September as in the previous years.

Jubb [15] noted outbreaks of poliomyelitis in West Kirby in three successive years—1912, 1913, 1914—one, seven, and four cases respectively. Roth [24] described a small epidemic in Oxfordshire in 1913, and Pim [22] another small epidemic in Dorset in 1914. Cases were also reported in co. Tyrone in 1914 [13].

The charts prepared from the notified cases of poliomyelitis during the past four years, both in London and the whole of England, show

that the disease has pursued the even tenor of its way with the usual seasonal incidence. There is no reason to believe that its prevalence has been greater or less than it was in years previous to notification. The chart (fig. 10) shows that the prevalence was in London somewhat greater in the year 1913 than in 1914 and 1915. In the year 1915 it is noteworthy that the maximum number of cases occurred not in August, or September, but in October.

(6) *Distribution of Cases in London.*

The study of the distribution of cases in the London area as indicated on the maps (fig. 11) would seem to point to the fact that the districts of Stepney, Islington, Hackney and Wandsworth have an exceptional incidence of the disease.

In 1913, Islington had 19 cases, Hackney 15, Wandsworth 14, and Stepney 14. In 1914, Islington had 8 cases, Wandsworth 2, and Stepney 27. In other districts there is a general evenness of distribution.

In 1914 the exceptional incidence of poliomyelitis which occurred in the East End of London (Stepney, 21 cases; Poplar, 5 cases; Bethnal Green, 5 cases—it will be noted that these figures do not accurately correspond to the notified cases, but the discrepancy is probably due to corrections of the notified returns) was investigated by Brincker [5], but he could determine no common factor. It was noteworthy that eighteen of the thirty-one cases were notified from the London Hospital. The Hospital authorities also observed that during the period when so many cases of poliomyelitis were under treatment a number of other patients were found to be suffering from herpes zoster.

It is quite certain that the number of cases notified does not represent the full extent of the prevalence of the disease in London. It is a well-recognized fact that not a few cases of the disease, when admitted to hospital, have not been notified.

As Dr. Newsholme points out: "Although the disease is under close scrutiny by many observers in different parts of the world, there are many etiological and epidemiological problems associated with it which still require elucidation," and he invites the co-operation of the medical practitioners in attendance on the case and the local medical officer of health.

The problem is one which will need a yet larger association of workers, not only the above, but also of those versed in animal

POLIOMYELITIS LONDON 1912. JAN.1 1912 - DEC.31 1912

FROM L.C.C. RETURNS

130 CASES NOTIFIED



POLIOMYELITIS LONDON 1913 JAN.1 1913 - DEC.31 1913.

FROM L.C.C. RETURNS

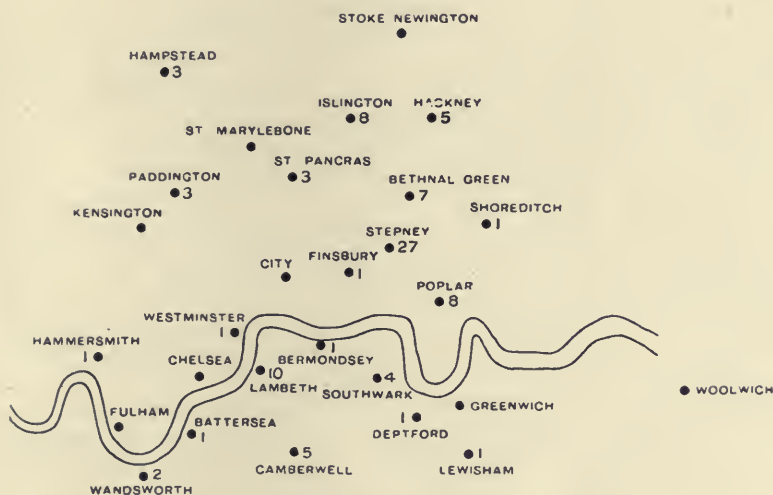
145 CASES NOTIFIED



POLIOMYELITIS LONDON 1914 JAN.1 1914 - DEC.31 1914.

FROM L.C.C. RETURNS

93 CASES NOTIFIED



POLIOMYELITIS LONDON 1915 JAN.1 1915 - DEC.31 1915

FROM L.C.C. RETURNS

100 CASES NOTIFIED



FIG 11.—A series of maps of the London District for the years 1912-13-14-15, showing the distribution of cases in various areas.

disease, having a knowledge of the method of neurological investigation, both clinical and pathological, and skilled in bacteriological and experimental investigations.

CHAPTER II.—PATHOLOGICAL ANATOMY.

Most observers of the present day regard the essential pathological change which occurs in acute poliomyelitis as an inflammation of the interstitial tissue of the central nervous system. This view has only been arrived at by the careful investigation of numerous observers in every stage of the disease. As methods of preparing and staining tissue improved, so the pathological picture has become more definite, and the views of pathologists as to the nature of the process, which at first were divergent, have become more in accord.

The leading points in the history of the advance of knowledge in this branch of the subject may be briefly stated as follows:—

Heine [38], in 1860, from clinical observation and deductive reasoning, came to the conclusion that the site of the lesion in poliomyelitis must be in the spinal cord.

In 1863 Cornil [35] investigated a case of poliomyelitis of forty-seven years' duration, and found considerable atrophy of the ventro-lateral columns and atrophy of the cells of the anterior horn. He did not, however, attach importance to the latter observation.

Then followed the observations of Prévost and Vulpian (1865) [42], who noted atrophy of the anterior horns and diminution in the number of ganglion cells, as well as atrophy of the anterior and lateral columns. Lockhart Clark (1868) confirmed this observation.

In 1870 Charcot and Joffroy [34] made an examination in a woman, aged 40, who had been paralysed for thirty-three years, and found absence of the ganglion cells, and attributed the atrophy of the muscles to the destruction of these trophic cells. They inferred a primary affection of the ganglion cells, and looked upon the interstitial change as a secondary reaction.

In 1871 Roger and Damaschino [44] demonstrated marked changes in the vessels, with cell proliferation in the anterior horns in more recent cases, and the question of a primary parenchymatous or primarily interstitial process was raised, and left for the time unanswered. Similar observations were published by Charleswood Turner, Frederick Taylor and Drummond in this country.

In 1888 Rissler [43] showed by the examination of acute cases that

the disease consisted in a disseminated infiltration and inflammatory process, which may attack any portion of the central nervous system, but showed a predilection for the grey matter of the spinal cord; but even he contends that the cells are primarily affected and the interstitial changes are secondary. He was the first to show that the pia mater might be involved.

The discussion between primary parenchymatous and primary interstitial process was carried on between numerous observers. Some pointed out the possibility of a simultaneous affection of both the parenchymatous and interstitial elements. The same process was shown to occur in both children and adults.

A series of observers now investigated acute cases, and most of them adopted the interstitial theory. In 1905 Wickman examined a number of acute cases, and in 1910 published further series. He confirmed the work of earlier observers that the process was not limited to the spinal cord, but occurred in a disseminated form in the medulla, pons, cerebrum, cerebellum, and membranes. The variation in the intensity of the process depends upon the varying richness of blood supply to the parts. The process is mainly interstitial and of the infiltrative lymphocytic type. The infiltration follows the distribution of vessels, and inflammatory oedema plays some part. Wickman considers that within the nervous system the inflammation travels along the perivascular lymphatics; the perineural lymphatics probably carry the infection from the site of inoculation to the spinal cord. Since Wickman's pathological investigation numerous workers have carried out observations on acute cases. Harbitz and Scheel consider that the infection is carried to the central nervous system by the blood as well as by the lymph-stream.

Forssner and Sjövall [37] noticed the rôle played by the phagocytes in the destruction not only of the ganglion cells but also in the spinal root ganglia, and Wickman and all recent observers confirm this observation [47].

Farquhar Buzzard, in his Goulstonian Lectures of 1907 [33], discussed the various views which had been advanced to explain the changes observed in the spinal cord. It is unnecessary to repeat these, but his conclusions in the light of recent investigation as to the nature of acute poliomyelitis, based on pathological observations, are of interest, for he says: "It is an acute specific fever occurring sporadically and epidemically; its essential lesion is an inflammation of the interstitial tissue of the central nervous system, due to the presence of micro-organisms, or their toxin, probably in the blood, but possibly in the lymph, circulating within that system."

I have already referred to the very complete observations of recent writers as to the nature of the lesion of poliomyelitis. In dealing with this part of the subject my description will be based mostly on my personal observations of human cases, not that they have been more extensive or complete than those of others, but that they are personal, and therefore more pertinent to these lectures. Endeavour has been made to include all stages and situations of the disease, and where individual observation was lacking, resource has been had to the work of others.

The changes are similar to those found in the experimental disease, *except* such as are described by Kling, Pettersson and Wernstedt [39] under the head "degeneration." Some cases of toxic neuritis show changes similar to those described by these observers, but the proof is lacking that they were cases of poliomyelitis.

Macroscopic Changes.

It may be said that the macroscopic changes observed in the body in a child dying of poliomyelitis are usually slight. Most observers have noted enlargement of the spleen, the thymus and lymphatic glands.

Flexner, Peabody and Draper [36], in 1912, had the opportunity of investigating the organs of ten children who died between the third and eleventh day of illness. Apart from the nervous system upon which the main injury is inflicted, all the cases showed hypertrophy of the lymphoid tissues. The affection of these was widespread, and included the tonsils, small intestine, thymus, and the superficial and deep lymphatic glands. The spleen was enlarged, and the Malpighian bodies prominent. The lesion in the liver consists of hyaline focal necrosis of liver cells, followed by regeneration and invasion by lymphoid cells and polynuclear leucocytes. They consider that the polymorphonuclearcytosis of epidemic poliomyelitis is caused not only by the lesion of the nervous system, but also by lesions of the lymphatic tissue and liver. This consideration will serve to explain certain discrepancies in the cell counts in the cerebrospinal fluid removed by lumbar puncture and in the circulating blood.

The cerebrospinal fluid is clear, and no change can be noted in the pia mater or pia arachnoid. On one occasion hæmorrhage in the lumbar region was found in an acute case, but it is possible that such was due to the lumbar puncture which had been performed.

The surface of the brain appears in most cases normal, but in one case of encephalitis with hemiplegia there was obvious congestion of the

vessels on the surface. The cord may on palpation, if the disease has been extensive, feel soft, but as a rule no alteration can be noted. In long-standing cases the cord may appear somewhat shrunken, and the grey and atrophied appearance of the ventral roots, as compared with the dorsal roots, is a marked feature. On section through the cord the grey matter, especially in the region of the anterior horn, appears hyperæmic, and in some cases the whole horn may appear filled with blood. Although the hyperæmia chiefly affects the anterior horns, yet it is not limited to this portion of the grey matter. Small dark lines are seen in the white matter, indicating congested vessels, but the white matter generally appears normal.

In cases of long standing, three months or more, the grey matter has a softened and gelatinous appearance, and on section this shrinks away from the level of the section, so that there is a depression in the region of the anterior horn. In the old and long-standing cases the whole cord may be shrunken on one side, and the grey matter especially may appear obviously smaller than that of the other.

In the medulla, pons and brain, areas of congestion similar to those seen in the spinal cord may be observed, and in long-standing cases a cavity may exist in the brain, as shown by White and Worthington [46].

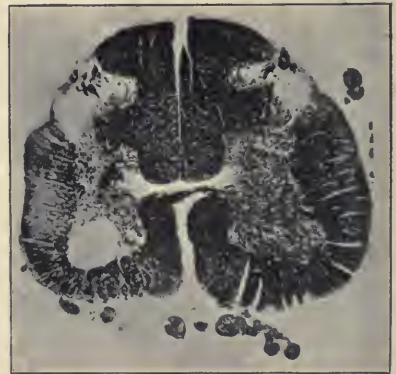
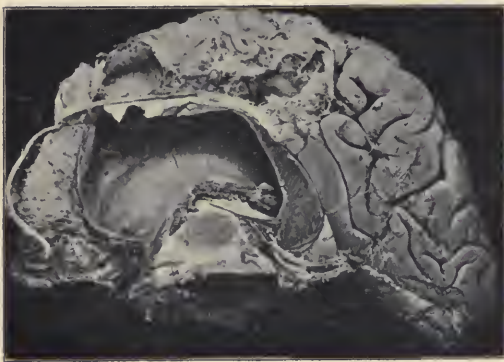
Rossi [45] describes a similar pathological condition in a case of poliomyelitis associated with an encephalitic process in the frontal, paracentral lobule and the corpus callosum. The case was that of a man who died at the age of 40. He had, when 6 months old, convulsions, followed by a paraplegia. The fits never recurred. He did not gain the power of walking. The right leg presented the typical condition of spastic paralysis with flexion of the knee and adduction of the thigh. In the left leg there was an almost complete flaccid paralysis, with wasting of muscles and shortening of the limb. Vasomotor troubles were present, and the reflexes were diminished in the left leg. The pathological examination showed in the cerebral hemisphere a condition of softening to the right and left of the mid-line with dilatation of the anterior portion of the left lateral ventricle. The cord in the lumbar region showed the typical appearance of an old poliomyelitis (figs. 12 and 13).

Microscopic Changes.

These will be described in three stages: (1) the acute, (2) the chronic, (3) the atrophic stage. There is, of course, no hard-and-fast

line of distinction between these stages, but specimens may be taken from cases dying within the first month as illustrative of the acute stage, two or more months after the acute onset as illustrative of the second, and two or more years after acute onset as illustrative of the third stage.

(1) *The acute stage.*—In a certain number of cases the pia mater is found to be infiltrated with small round cells: these cells are generally most numerous around the vessels in the anterior median fissure and



FIGS. 12 and 13.—Photographs of brain and spinal cord, showing a cerebral and a spinal lesion, resulting from poliomyelitis in early life.

Reproduced from the *Nouv. Icon. de la Salpêtrière*, 1907, by the kind permission of Mon. Italo Rossi and Mon. H. Meige.

may be limited to this region (fig. 15). Sometimes the infiltration extends on to the posterior surface of the cord and involves the posterior roots, but often it is limited to the anterior region of the cord.

I do not propose to enter into the discussion as to the nature and origin of these cells, either here or in the spinal cord, but shall be content to designate them lymphocytes or infiltration cells. The whole cytology of the infiltration of the vessel walls, the soft membranes and the grey matter is discussed by Buzzard [33], Wickman [47], Mackintosh and Turnbull [40], Barnes and Miller [28], and Kling, Pettersson and Wernstedt [39]. Buzzard describes five varieties of cells in the infiltration of the grey matter, and says: "Excluding all these cells, there are still a considerable number which it is difficult to classify, and for this reason it is impossible to gauge accurately the relative proportion of the various elements. My general impression is that neuroglial proliferation and lymphocytic infiltration are the most



FIG. 14.—Lumbar region of cord of a child who died on the twenty-eighth day after onset of illness, showing extreme vascular congestion and infiltration of the grey matter most marked in the region of the anterior horns.

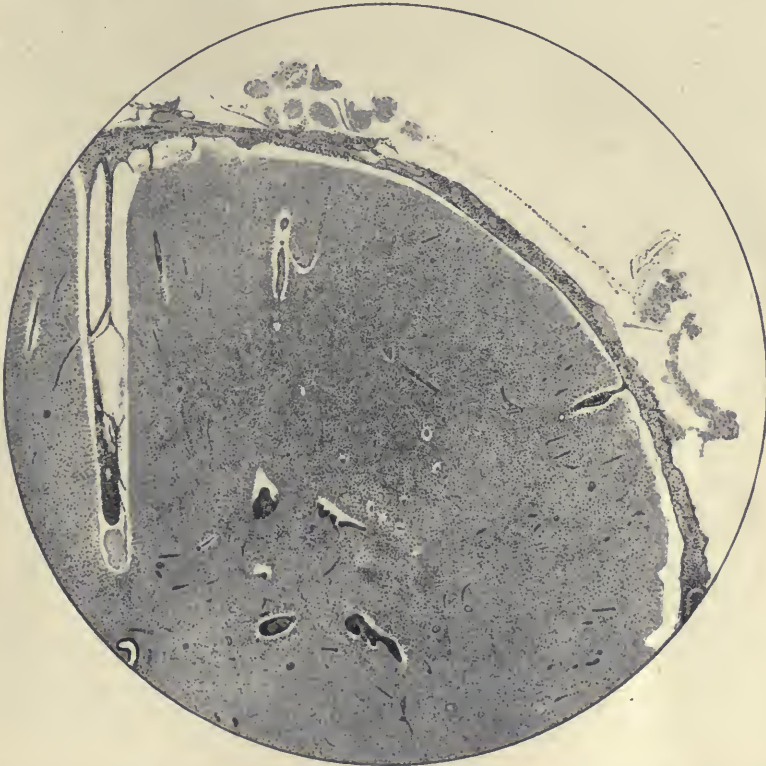


FIG. 15.—Section of spinal cord of a child who died on the ninth day of illness, showing infiltration of the grey matter, perivascular infiltration and invasion of the pia arachnoid membrane. Note that the cells of the anterior horn can still be seen in the infiltrated area.

prominent factors in the production of these cell masses." Mackintosh and Turnbull describe seven varieties of cells.

Spinal cord: The appearance of the spinal cord when stained by the Van Gieson method is very striking (fig. 14): the vessels, and especially those in the anterior median fissure, are dilated and surrounded with small round cells, and the grey matter in the regions of the anterior horns is infiltrated with these cells (fig. 15). The white matter shares to a limited extent in this infiltration, as do also the vessels passing from the pia into the cord, which is in the case figured markedly involved on the anterior surface (fig. 16).

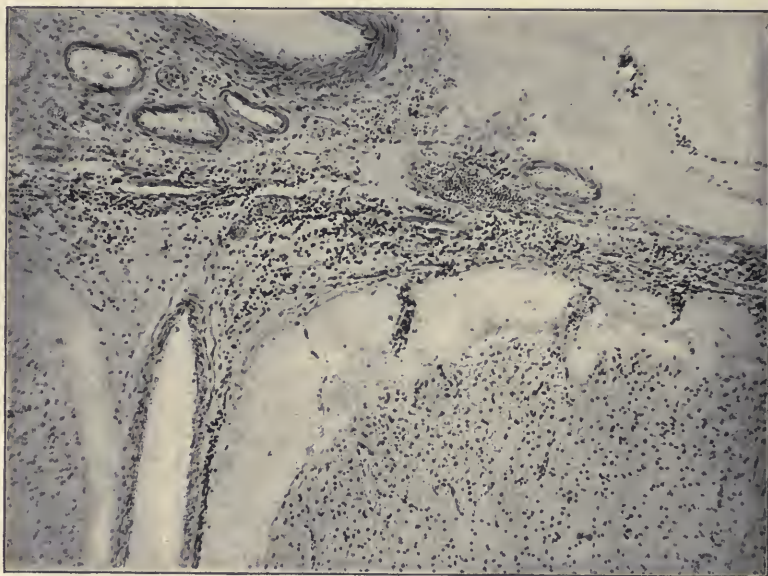


FIG. 16.—Photograph of the same section of spinal cord under high magnification to show small-celled infiltration of the layers of the pia lying next to the spinal cord and the perivascular infiltration of the vessels passing into the cord.

Extravasations of blood, large and small, can be seen in the grey matter, mostly in relation to vessels, both veins and arteries. In later stages of the disease the vessels may appear thrombosed; in the earlier stages there is no evidence of this, though at one time I regarded thrombosis as a cause of the softening [31]. In the grey matter, when the infiltration has not been too extensive, the large cells of the anterior horn can be seen—some of them present a normal appearance, some are surrounded by infiltration cells, and others, again, are being destroyed by phagocytic neuroglia cells (neuronophagia) (fig. 17). Some of the

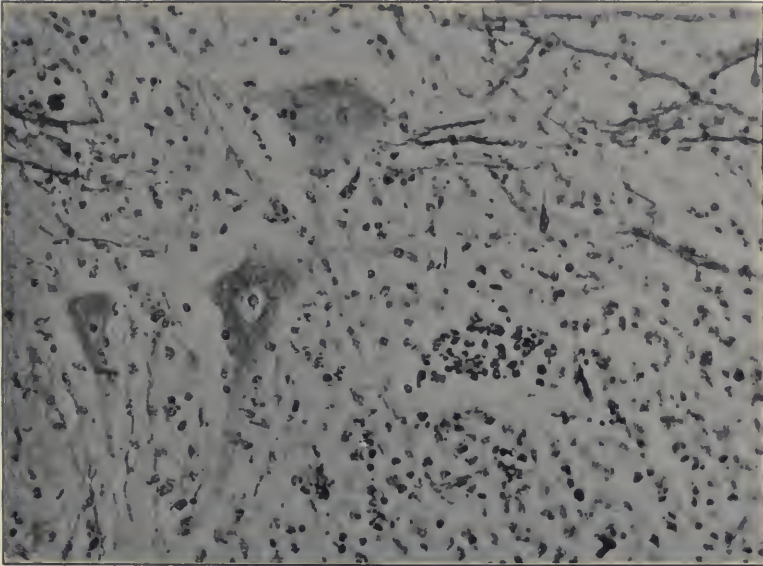


FIG. 17.—Photograph of the ganglion cells of the anterior horn of the same case, showing varying degree of "neuronophagia." Note (i) the cell with a distinct nucleus and nucleolus, with "neuronophagic" cells adherent to the wall, (ii) the cell with indistinct nucleus and "neuronophagic" cells within its substance, and (iii) a cell wholly replaced by "neuronophagic" cells.



FIG. 18.—Section of medulla and fourth ventricle taken from a child who died forty-eight hours after onset of disease, showing extreme congestion and perivascular infiltrations of vessels and lining membranes of the fourth ventricle; there was also extensive poliomyelitis of the spinal cord.

ganglion cells are entirely replaced by neurophagic cells. Portions of the grey matter other than the anterior horns may be affected, and the changes are similar.

The posterior root ganglia show the same cellular infiltration and cytological changes. Flexner states that experimentally lesions of the ganglia are as common and constant as the lesion of the grey matter, and in man are probably as constant, but not so frequently looked for.

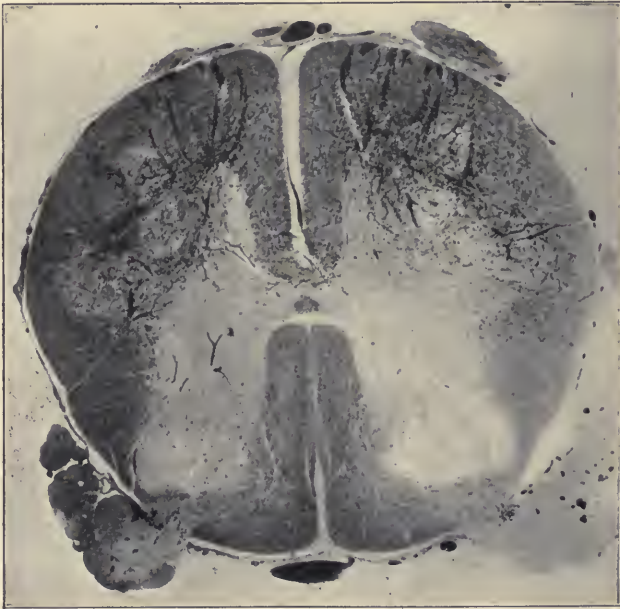


FIG. 19.—Section of spinal cord of a child who died six weeks after the onset of the disease, stained by Marchi method, showing degeneration of the efferent fibres of the anterior roots.

In the medulla and mid-brain changes similar to those in the spinal cord can be observed, and these are present in cases which, during life, have exhibited no marked bulbar or pontine symptoms. In the specimen shown (fig. 18) the poliomyelitic changes are most marked in the region of the fourth ventricle and invade the lining membranes of that cavity. The boy from whom this specimen was taken rapidly passed into coma and died in forty-eight hours.

One interesting case of facial paralysis on one side is on record in which the seventh nerve nucleus on that side was destroyed, while that on the opposite side was unaffected [30].

(2) *Chronic stage*.—The study of the changes in the spinal cord

during the chronic stages is of considerable interest. They show the local destructive lesion giving rise to necrosis, to secondary degeneration taking place in the efferent portions of the anterior root, and to degeneration of antero-lateral tracts in the spinal cord resulting from these lesions (fig. 19). In general, the lesion is too diffuse to be of much service for tracing the endogenous fibres of the cord, but Mott [41] has

FIGS. 20, 21, 22.—A series of three sections taken from the lumbar cord of a child who died seven weeks after the onset of the disease: (i) stained by Marchi method; (ii) by Weigert Pal method; and (iii) by Van Gieson method.



FIG. 20.—Gives a positive picture, the degenerated myelin and the fat in the cells in the perivascular space being stained black.

been able to trace such in one case, and Holmes and myself [32] were able to trace the intra-medullary course of the spinal portion of the spinal accessory nerves in another.

During this stage the changes are best shown by the Marchi and Weigert-Pal method. The Marchi stains the degenerate myelin tissue black, whilst the Weigert-Pal stains the normal fibres a dark blue. Positive and negative pictures are therefore presented respectively.

Fig. 20 represents a section through the lumbar region of the cord and shows an area of necrosis, limited to the external portion of the anterior horn. The vessels are stained black, owing to the loading of the perivascular lymphatics with the products of degenerated myelin. In the antero-lateral tract of the spinal cord numerous black dots can be seen, representing degenerated fibres.

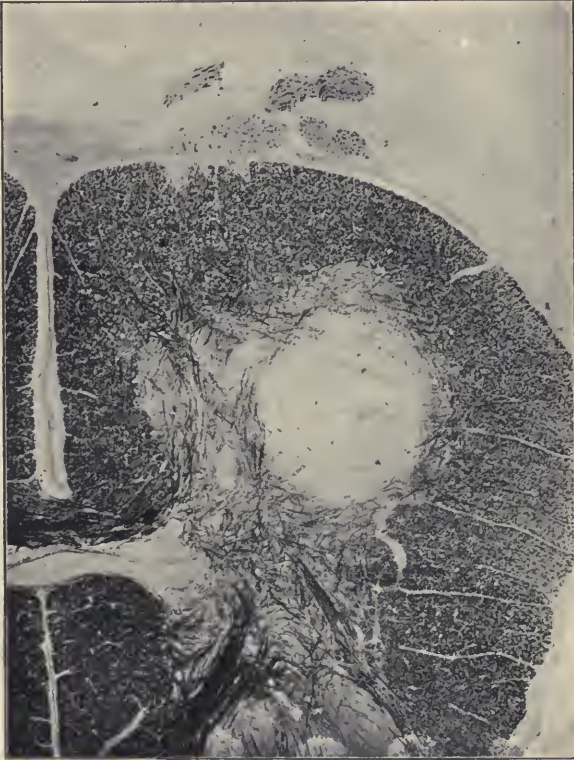


FIG. 21.—Gives a negative picture, the area of complete degeneration being white—the number of the medullated fibres in the grey matter of the anterior horn is diminished.

If this positive picture is compared with the negative picture presented by the Weigert-Pal method (fig. 21), it is clear that the destruction of tissue is widespread, and in some directions more extensive than that presented by the positive picture. The myelin sheaths have been destroyed for a considerable distance beyond the necrotic area, so that practically the whole of the anterior horn is involved, though not to the complete extent to which the external portion has suffered. The products of degeneration have to a considerable extent been removed from the peripheral portions of the lesion.

The specimen stained by hæmatoxylin (fig. 22) shows the remains of the inflammatory process and the formation of new tissue.

(3) *Atrophic stage* (two years or more).—In the *atrophic stage* the products of necrosis become absorbed—the anterior horns undergo shrinking, and the whole of the grey matter on the affected side becomes atrophied. The white matter also suffers, but relatively less than the



FIG. 22.—Gives a positive picture, the glia tissue with but few cellular elements taking the place of the degenerated tissue.

grey matter, and the whole of the anterior lateral tracts of the cord are pale and diminished in size, and in some cases a sclerotic area is left in the anterior horn (fig. 13).

Peripheral nerves : In the acute stage, cell infiltration can be found in the peripheral nerves (fig. 23), but it is difficult to say that such infiltration produces any symptom or pathological effect. The observations on the point are not extensive, and need further investigation. The

specimen (fig. 23) is taken from the anterior crural nerves of a boy, aged 5, who died on the ninth day after the onset of acute poliomyelitis. In long-standing cases the Marchi method shows the usual degeneration of the efferent fibres. The Weigert-Pal method shows that the number of normal fibres left in a degenerated nerve is very considerable: such fibres are usually of large size, and are probably largely afferent in function. No true interstitial change can be found in the nerves.

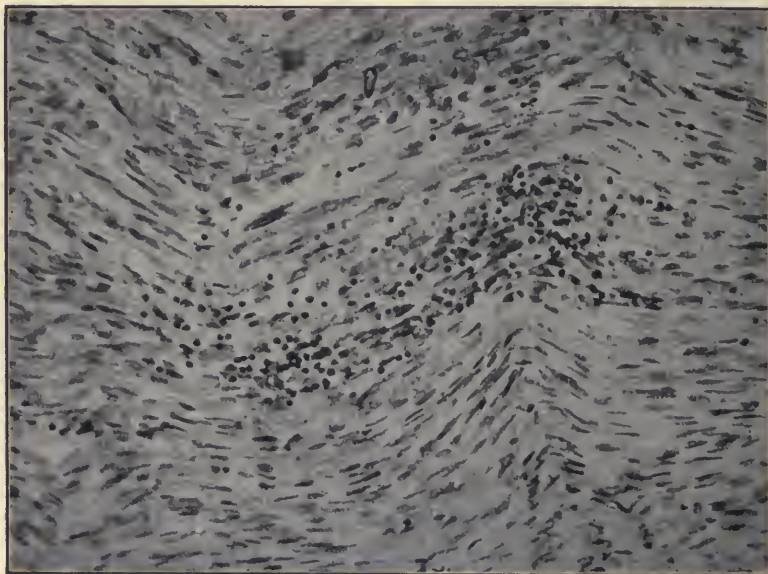


FIG. 23.—Longitudinal section of anterior crural nerve of a boy who died on the ninth day of the disease. The specimen shows round-celled infiltration of the nerve.

Muscles: The study of the muscle in the chronic and late stages of the disease is of interest. A muscle which is not wholly degenerated shows normal muscle-fibre alongside with fibres and bundles of fibres which have undergone complete degeneration and been replaced by fibrous tissue. In those cases in which the muscles have undergone complete fibrous or fatty degeneration, it is interesting to note that the muscle-spindles still exist [29], and contain a normal and well-striated muscle-fibre and a normal nerve. It is a striking fact that certain muscles seem to undergo a fibrous degeneration; whilst others undergo a fatty degeneration. As an instance of this former may be mentioned the biceps, as an instance of the latter the gastrocnemius.

In concluding this review of the pathology of the subject, it may be

said that so far as our present knowledge goes the pathological picture above presented is (with the exception of rabies) distinctive of the virus of poliomyelitis.

CHAPTER III.—EXPERIMENTAL POLIOMYELITIS.

(1) *Earlier Experimental Work.*

In 1909 Landsteiner and Popper succeeded in transmitting poliomyelitis to two monkeys, but failed to propagate the experimental disease beyond the first generation. In the same year Knöpfelmacher and Strauss and Huntoon in America were also successful in producing the disease in monkeys by injecting into the peritoneum an emulsion of the spinal cord from cases of poliomyelitis.

Flexner and Lewis, in 1910, overcame the difficulty of propagation by substituting intra-cerebral for intra-peritoneal injection, and were the first observers to transmit the disease through a series of monkeys. As Flexner points out, the choice of an intra-cerebral route as superior to the intra-peritoneal route was not haphazard, as all the severe effects of poliomyelitis are inflicted on the nervous system, and, upon reflection, this fact at once suggested that the parasitic cause of the disease must find favourable conditions for multiplication within the nervous tissues [49].

Landsteiner and Levaditi showed that the virus would pass through porcelain filters and also that glycerine did not destroy it. Working on the same lines and at the same time, Leiner and Wiesner in Vienna, Roemer and Joseph in Marburg, Krause and Meinicke, confirmed these observations and added much to the knowledge of the nature of the virus [48], [50].

(2) *Properties of the Virus.*

(a) *Filterability.*—It was shown by Flexner and Lewis and Landsteiner and Levaditi that the virus would pass through a porcelain filter. The latter observers noted that it would pass through the Berkefeld, Chamberland, Reichel and Pukall filters, but that, after such a passage, the virus lost some of its virulence, and the incubation period was always prolonged, and the monkey either did not die or only died some days after the development of the disease.

(b) *Glycerine resistance.*—It has been shown by Landsteiner and Levaditi that the virus will resist the action of glycerine either concentrated or with 50 per cent. of water without impairing its

virulence. The virus has been kept by Flexner for twenty-five months in glycerine at a temperature of 4° C. without affecting its virulence. In this respect it resembles that of rabies and vaccinia.

(c) *Resistance to drying*.—Flexner and Lewis, Landsteiner and Levaditi, found that prolonged drying, even for twenty-four days, at a temperature of 22° C. did not diminish the virulence, so that in this respect it differed from rabies. Leiner and Wiesner, however, found that drying of thin films for four hours at a temperature of 37° C. did destroy the virulence. They showed that the virus is killed by exposure to a temperature of 55° C. for half an hour, and it is not killed by exposure to a temperature of -8° C. Flexner found that long exposure (eighteen to thirty-six months) to a temperature of -2° C. to -4° C. did destroy the virulence of the virus.

(d) *Resistance to disinfectants*.—It has been shown by Landsteiner and Levaditi that 0.2 per cent. solution of potassium permanganate will kill the virus in one hour at a temperature of 39° C., and that 6 per cent. peroxide at the same temperature will destroy the virus in forty-five minutes. The virus is not killed by $\frac{1}{2}$ to $1\frac{1}{2}$ per cent. of carbolic acid.

(3) *Cultivation of the Organism.*

In October, 1913, Flexner and Noguchi [59] published the method by which they had succeeded in cultivating the organism of poliomyelitis under anaerobic conditions in ascitic fluid to which fresh rabbit's kidney has been added.

The micro-organism consists of globoid bodies measuring from 0.15 μ to 0.3 μ in diameter, and arranged in pairs, chains and masses, according to the condition of growth and multiplication. The chain formation takes place in a fluid medium, the other grouping in both solid and fluid media. Within the tissues of infected human being and animal, the chains do not appear. Whether the micro-organism actually belongs to the bacteria or to the protozoa has not been determined, but it is pointed out that the organism is associated with the production of an acute disease in which suppuration does not form a prominent part.

The experimental disease caused by the inoculation of cultures resembles that produced by the virus of poliomyelitis as ordinarily employed. The cultivated micro-organism withstands the action of glycerine, passes through the Berkefeld filter, and the filtrates yield, upon recultivation, the particular organism contained within the filtered culture. By employing suitable staining methods the micro-organism

can be detected in film preparations and in sections of nervous tissue from monkeys infected with cultures. The organism thus fulfils the condition hitherto demanded for the establishment of causal relations between an extraneous parasite and a specific disease: The micro-organism exists in the infectious and diseased organs; it is not, so far as is known, a common saprophyte or associated with any other pathological condition; it is capable of reproducing on inoculation the experimental disease in monkeys, from which animals it can be recovered in pure culture. Besides these classical requirements, the micro-organism withstands preservation and glycerination, as does the ordinary virus of poliomyelitis within the nervous organs.

Flexner and Noguchi, in conjunction with Amoss [51], [60], have now continued their investigation of the organism further, and having carried the strain through twenty subcultures have proved that the final culture was pathogenic to monkeys.

The micro-organism isolated from poliomyelitic tissues may possess pathogenic properties after having been cultivated artificially for a period of a year or more, and after an almost indefinite degree of dilution of original nervous tissues from which it was derived.

The micro-organism cultivated from poliomyelitic tissue is adapted with difficulty to saprophytic conditions of multiplication, but once adapted growth readily takes place upon suitable media. When, however, as a result of inoculation into monkeys the parasitic propensities of the micro-organism are restored, it again displays the same marked fastidiousness to artificial conditions of multiplication present at the the original isolation.

Flexner, Noguchi, and Amoss end their paper with the following guarded conclusions:—

That the experiments afford additional strong evidence in support of the view already expressed that the micro-organism bears an etiological relationship to epidemic poliomyelitis in the human subject, and to experimental poliomyelitis in the monkey.

(4) *Method of Infection.*

The emulsion is prepared by pounding up 1 grm. of the infected portion of the spinal cord with 20 c.c. of normal saline solution; 0·5 c.c. of this emulsion is injected into the brain and 4 c.c. to 5 c.c. into the peritoneal cavity (Roemer). The amount of virus required is extremely small—viz., less than $\frac{1}{1000}$ c.c. of a 2·5 suspension of spinal cord.

The most certain method of producing infection is by injection of

the virus into the brain. Injection into the peritoneal cavity, the anterior chamber of the eye, the subcutaneous tissue, intraspinal, intraneural, and intravenous injections have all been successful in producing the disease.

It has been shown (Flexner and Lewis, Levaditi and Landsteiner) that the virus injected into a peripheral nerve gives rise to paralysis, the disease commencing in the limb corresponding to the nerve injected.

Leiner and Wiesner found that if the nerve is divided immediately after the introduction of the virus into the peripheral end, the spread of the disease is prevented. In whatever way the animal is infected it is in the central nervous system, and especially the grey matter of the cord, that the virus tends to locate itself.

Leiner and Wiesner showed that the virus could pass through the gastro-intestinal mucosa, but other observers, Levaditi and Landsteiner, failed to obtain positive results, and suggest that infection only takes place if there is a previous lesion of the intestinal walls. Leiner and Wiesner, in order to avoid the action of gastric juice, injected the virus into certain portions of the intestines after opening the abdomen. Three of the four monkeys thus operated on developed poliomyelitis. Flexner, Clarke and Dochez showed [57] that the virus could survive the action of both the gastric and intestinal secretions.

The virus will pass the nasal mucous membrane if injured (Landsteiner and Levaditi), but Leiner and Wiesner have shown that it will pass the uninjured mucous membrane. Natural contagion has been reported in a monkey which was kept in a cage in which the virus had been smeared over the bars; non-infected monkeys have been kept in close contact in the same cage with infected monkeys without contracting the disease (Levaditi and Danulesco [65]).

The great epidemic of poliomyelitis in Sweden, in 1911, gave the observers Kling, Pettersson, and Wernstedt [64] the opportunity of an investigation on somewhat different lines from those previously adopted. They obtained washings from the mouth, nose, pharynx, upper air-passages, and small intestine of a number of patients—(1) dead of the disease; (2) living cases; (3) abortive cases; (4) healthy persons in contact with infected individuals. Washings from these mucous membranes were filtered through a Heims asbestos filter, and by a combined intraperitoneal injection with an inoculation into one sciatic nerve of the filtrate they succeeded in infecting monkeys.

(1) *Dead of the disease.*—Out of fourteen patients dead of poliomyelitis thus investigated, in only one were the authors unsuccessful in demonstrating the presence of the virus of poliomyelitis.

It is, however, interesting to note that the changes in the spinal cord, which have been considered most characteristic of poliomyelitis—i.e., cellular infiltrations—were not always present. In fact, out of fifty-nine monkeys which were infected from typical cases of poliomyelitis, twenty-five—i.e., 42 per cent.—showed infiltrative changes, and thirty-four—i.e., 58 per cent.—degenerative changes.

(2) *Living cases of poliomyelitis.*—Having obtained results from persons dead of poliomyelitis, the authors next proceeded to investigate the secretions from living persons, and they obtained material from the mouth, nose, pharynx, and large intestine of twelve living persons suffering from poliomyelitis. In only one case did the observers fail to infect the monkeys.

Thus the presence of the microbe has been detected in the secretions of one of the examined membranes—i.e., mouth, nose, upper air-passage, or intestine—in twenty-four out of twenty-six cases.

Considering the difficulty of infecting monkeys in every instance, the observers consider themselves fully justified in drawing the following conclusion, viz., that the virus in all probability is always present in the mucous membranes of the nose, mouth, pharynx, and the intestine of persons affected by poliomyelitis during the acute stage of the disease.

(3) *Abortive cases, and (4) healthy persons in contact with infected individuals.*—Having obtained results from persons suffering with definite poliomyelitis, the authors proceeded to investigate the washings from the mucous membranes of abortive cases and healthy persons. In a family of five, one of whom had definite poliomyelitis, two an uncertain illness of short duration, and two had remained well, they showed that three carried the microbe of poliomyelitis in their mucous membranes—viz., the one who had distinct paresis, one of those who had had an abortive attack and one of those who had had no illness.

The existence of the micro-organism of poliomyelitis has been demonstrated also in the secretion from the mouths of three persons who had not, as far as is known, had any contact with patients showing definite paresis, persons whose illness was characterized by such vague symptoms that only in one case did the suspicion arise that some form of poliomyelitis was present.

In six families the experimental method has demonstrated the existence of carriers of the virus in several members of the family, only one person in each family having typical paralysis. It is therefore probable that virus carriers are very common.

Flexner, Clark and Frazer [58], dealing with passive human

carriage of the virus, demonstrated its presence in the throats of the parents of a child suffering with the disease and confirm in this respect the above observations.

Intraspinous infection.—So far no one has detected the virus in the cerebrospinal fluid in human cases of poliomyelitis, and it is usually absent in the spinal fluid of monkeys at the time of the onset of paralysis, although it may be present at an earlier period after intracerebral inoculation.

Flexner, and Clark and Amoss [52] [54], carried out a series of experiments of infecting monkeys by the method of intraspinous injection of the virus. They experienced no great difficulty in securing infection by this route, although somewhat larger doses of an active virus were required. The virus could be demonstrated in the sub-arachnoid spaces for forty-eight hours after injection, but it was no longer present on the sixth day, at the time when the first symptoms of infection had made their appearance. The failure of the cerebrospinal fluid from human and experimental cases of poliomyelitis to produce the disease when inoculated into monkeys is due to the fact that the virus is either fixed by the nervous tissue or has passed into the blood, which tends to destroy it.

Propagation of the virus by the blood-stream.—It is recognized that the intravenous method of inoculation, even when such large quantities as 50 c.c. to 100 c.c. of the virus are used, is an uncertain and inconstant method of producing infection, although so small an amount as 0.5 c.c. of the same virus succeeds when introduced into the brain. It has also been shown that when infection does occur the incubation period is greatly delayed, in one instance to nineteen days, and during this period the cerebrospinal fluid contained the organism [53].

Flexner and Amoss [54] have made a careful study of this point, and by a series of experiments they trace this discrepancy to the apparent inability of the virus to enter directly the substance of the brain and spinal cord from the blood.

In order to reach these organs the virus must leave the blood and pass into the cerebrospinal fluid, and this it can only do if the choroid plexuses are rendered unduly penetrable, either by excessive doses of the virus or by aseptic inflammation produced by the injection of horse serum.

In the passage of the virus through the cerebrospinal fluid they have shown that it is possible to prevent infection by the injection of an immune serum in the sub-arachnoid space by lumbar puncture. The

virus when injected into the blood is deposited promptly in the spleen and bone-marrow, but not in the kidney, spinal cord, or brain, but the inter-vertebral ganglia remove the virus from the blood earlier than does the spinal cord or brain. They believe that these experiments support the view that the infection in epidemic poliomyelitis in man is local and neural and by way of the lymphatics, and not general by way of the blood; hence they uphold the belief that the entrance is from the upper respiratory mucous membrane.

Incubation period.—The incubation period is subject to very considerable variations. The variations depend upon—(1) The method of injection; (2) the amount of virus given; and (3) the method of treating the virus before injection. Of eighty-one monkeys infected by Lewis and Flexner, forty-seven became paralysed between the eighth and the twelfth day, eighteen became paralysed before the eighth day, and sixteen after the twelfth day. Levaditi found the average incubation period from seven to ten days, and Roemer gives the incubation period as nine days.

In Kling, Pettersson and Wernstedt's series, although the incubation varies within very wide limits, yet the average duration works out at nine to ten days.

The following factors were found to govern the incubation period: The less virulent the material, the longer was the incubation period. Filtration diminished the virulence (Levaditi and Landsteiner, Leiner and Wiesner). Thus an unfiltered emulsion produced poliomyelitis in seven days; the same quantity of filtered emulsion produced poliomyelitis in twenty-seven days.

The quantity given also alters the incubation period. Dilution, again, has the same effect, and if diluted beyond a certain limit the virus will not produce poliomyelitis (Roemer). Thus an animal, injected intra-cerebrally with 0.5 c.c. of a 5 per cent. spinal cord emulsion, became paralysed on the seventh day and died on the eighth day. Another monkey, inoculated with the same quantity but ten times less concentrated, became ill on the twelfth and died on the thirteenth day. Another monkey, injected with the same quantity 100 times diluted, survived without having manifested any paralytic symptoms.

Leiner and Wiesner found that inoculation of a very concentrated virulent emulsion appeared to exercise rather an unfavourable influence on the development of poliomyelitis. The incubation period was slightly longer and the course of the disease goes on as if in the nervous tissues there were, in addition to the acting virus, certain preventive substances which exercised a neutralizing action on the virus.

What happens during the incubation period? Leiner and Wiesner showed that the virus spread to the nervous system before it was possible to observe any morbid manifestation in the central nervous system. Levaditi and Landsteiner found that the anatomical and pathological alterations commenced at a time very close to the outbreak of clinical signs. The virus of poliomyelitis can invade the nervous system and multiply there without causing for a time any apparent trouble or distinct lesion. The paralytic phenomena in a monkey may commence very suddenly—i.e., the monkey may be quite well in the morning and completely paralysed by the evening. It is a striking fact that in the majority of cases, in spite of the inoculation of the virus into the brain, the disease commences by paralysis localized to the lower extremities.

(5) *Immunity.*

On clinical grounds there is good reason to believe that an individual who has survived an attack of poliomyelitis is immune to a second attack. Experimentally it has been shown by Flexner and Lewis, Levaditi and Landsteiner, and Roemer that monkeys which have survived the acute period of infection are immune to a fresh dose of the virus. Roemer considers that immunity is only acquired after about the twenty-fourth day, but other observers do not confirm this observation.

In one case Leiner and Wiesner have been able to reinfect a monkey which was paralysed for eighteen days. This is probably an exceptional instance. Leiner and Wiesner performed experiments to determine if the nervous system of monkeys, killed after the acute state had passed and the refractory stage reached, contained an appreciable quantity of active virus. They found that they could transmit the disease by using the spinal cord of a monkey killed on the twenty-fourth day of the disease. This would seem to show that the active virus and the antibodies can exist at the same time and in the same individual.

Production of artificial immunity.—Levaditi and Landsteiner used the same method for rendering a monkey immune against poliomyelitis as is used for producing immunity against rabies. To a certain extent this method was successful, but in some cases poliomyelitis has been produced by injection of the dried cords. Flexner and Lewis, by giving injections of diluted virus, were able to make monkeys immune to many times the lethal dose.

After recovery from poliomyelitis, both natural and experimental, it has been shown that an active immunity has developed. The state

of immunity is associated with the occurrence in the blood of principles that neutralize the virus. Netter and Levaditi showed this in human cases [68].

Flexner, Clark and Amoss [56] carried out a series of experiments to determine whether antibodies existed within the cerebrospinal fluid. It is known that antibodies are not secreted in appreciable quantities in the cerebrospinal fluid. The experiments show that the cerebrospinal fluid of convalescents tends to be devoid of the neutralizing immunity principles for the virus of poliomyelitis, although they may exceptionally be present within the fluid.

(6) *Experimental Investigations with the Object of Determining the Possibility of Transmission of Poliomyelitis by Means of Dead Objects and Flies.*

Flexner and Lewis, Landsteiner and Levaditi and Roemer found that prolonged drying, even for twenty-four days at a temperature of 22° C., did not diminish the virulence of the virus. Leiner and Wiesner, however, found that drying of the film for four hours at a temperature of 37° C. did destroy the virus. Landsteiner, Levaditi, and Pastia found that the virus remained potent in sterile milk and sterile water for at least thirty-one days.

Josefson succeeded in producing experimental poliomyelitis with a handkerchief and fancy work which had been in contact with a patient suffering from poliomyelitis. Neustaedter and Thro succeeded, after many failures, in producing poliomyelitis in a monkey with a filtrate of macerated dust collected from rooms in which cases of poliomyelitis had been nursed.

Howard and Clark [62] showed that the domestic fly can carry the virus of poliomyelitis in an active state for several days upon the surface of the body, and for several hours within the gastro-intestinal tract, and that the bed-bug has taken the virus with the blood from infected monkeys and maintained it in a living state within the body for a period of seven days.

Lice have not taken the virus out of the blood of monkeys or maintained it in a living state. Kling, Pettersson, and Wernstedt failed to communicate the disease by the means of fleas.

Rosenau, in 1912, demonstrated that poliomyelitis could be transmitted from monkey to monkey by the means of the bite of the stable-fly (*Stomoxys calcitrans*), and this observation has been confirmed by Anderson and Frost. These experiments are the more remarkable,

for it is a matter of some difficulty to infect a monkey with the blood of a patient suffering from poliomyelitis, and as a rule a considerable quantity is required.

Clark, Fraser and Amoss [53], in 1914, conducted a further series of experiments with *Stomoxys* which gave wholly negative results, and a second series conducted by Anderson and Frost were similarly negative, as were also those of Sawyers and Herms.

Francis [61] made an attempt to transmit poliomyelitis by the bite of *Lyperosia irritans* (a blood-sucking fly), but the experiments yielded entirely negative results.

The whole of the experimental evidence is strongly against the communication of the disease to man by the means of fleas, lice, bugs, and flies.

(7) *Variation in the Pathogenicity of the Virus.*

Flexner and Clark state that they have succeeded in implanting upon monkeys all ten strains of human virus which they examined. That is to say, monkeys have been infected from ten human cases. These authors state that other experimenters have only been able to implant about one-half of the human strains of poliomyelitic virus upon monkeys. In order to succeed in all instances, it is necessary to inoculate emulsions of the human spinal cord, and preferably to make double inoculation into the brain and peritoneal cavity.

English strains have only twice been implanted on monkeys: (1) Levaditi [66] in Paris, with material supplied to him by Gordon from the Cornish epidemic in 1911, succeeded in reproducing the disease from the spinal cords of three cases out of four sent to him; (2) McIntosh and Turnbull [67] in 1913 succeeded in two out of four cases from the London Hospital.

The human strains of the virus not only infect monkeys less readily than do the modified or monkey strains, but the experimental disease produced by them is less severe and less fatal. After the strains have once become wholly adapted to the monkey the paralytic disease appears in a more severe form and the degree of infectivity rises, so that exceedingly minute doses of a filtrate are capable of producing constant infection.

Flexner says the Swedish virus of 1911 appears to be the most powerful yet studied; this is indicated by the fact that saline washing of the nose, throat and intestine could be inoculated successfully after removal of all bacteria by filtration, in nearly every instance.

In America it has been difficult to procure infection with these materials, from which it has been concluded that the virus displays degrees of infectiveness to monkeys. This is further borne out by the difficulty of transmitting the sporadic English cases, as shown by McIntosh and Turnbull.

Natural Variation in the Pathogenicity of the Virus.

Flexner, Clark and Amoss [56] found that a strain of poliomyelitic virus propagated in monkeys for four years displayed during that time three distinct phases of virulence. At the outset the virulence was low, but by animal passage it quickly rose to a maximum; the maximum was maintained for about three years, when without known changes in the external conditions a diminution set in and increased until at the expiration of a few months the degree of virulence about equalled that present at the beginning of the passage in monkeys.

By resorting to the original specimen from which the virus was obtained a highly virulent strain was again produced. It is clear, then, that the frequent and long-continued passage through monkeys finally brings about a depression of virulence, whilst preservation in a state of latency for a period equally great exerts no depressing action.

The cycle of changes in virulence is correlated with the wave-like fluctuations in epidemics of diseases, which also consist of a rise, temporary maximum, and fall in the number of cases produced.

It is this variation in the epidemic which has led to the formulation of the hypothesis of concomitant causes of von Pettenkofer and of Nägeli.

Whilst the one supposes a necessary ripening of the microbic agent in the earth as a pre-requisite, the other invokes the co-operation of a second, although unknown but subsidiary, micro-organism. In these experiments of Flexner, Clark and Amoss we have an explanation of the wave of epidemic disease due to variation in the quality of the virulence of the micro-organism causing the disease.

(8) *The Clinical Picture of Experimental Poliomyelitis in Monkeys.*

The clinical picture of experimental poliomyelitis in monkeys as described by Landsteiner and Levaditi, Flexner and Lewis, and others is similar to that which occurs in man. In addition to the ordinary type of limb paralysis, the muscles of the face, the oculo-motor muscles may be paralysed, sometimes alone, sometimes in association with limb

paralysis, and Roemer has reproduced the "jump" type in monkeys, and relapses occur as a rare manifestation as in man. In view, however, of the pathological finding of Kling, Pettersson and Wernstedt [64], who stated that a considerable number of their cases showed degenerative changes, it is important to study the clinical picture in their cases. That the clinical picture of experimental poliomyelitis may vary is shown by Leiner and von Wiesner, who have described a type of slowly progressive weakness in monkeys which they have designated as "marasmic."

Kling, Pettersson, and Wernstedt have divided the 116 monkeys who suffered from poliomyelitis into six clinical groups: (1) an upper limb, (2) a lower limb, (3) a mixed, (4) cerebral and bulbar type, (5) general muscular weakness, (6) "found dead." The first four groups are so well known and correspond to the usual type in man that no comment is necessary (except that in only one monkey did the illness commence with cerebral symptoms). With regard to the "general muscular weakness" which the authors use as synonymous with the "marasmic type" of Leiner and von Wiesner, it has no known counterpart as a clinical type in man.

The feature of this "general muscular weakness" group is weakness without localized paresis, and the authors state that they have found the disease manifesting itself in this manner in no fewer than twenty-six out of the 116 cases.

A monkey (No. 140) inoculated on November 1 was noticed on November 16 to be more slow in its movements. By November 20 it moved somewhat joltingly, but was otherwise well, possibly weak in the fore-limbs on November 25. It has during the past days been huddled up in one spot, and to-day is lying at the bottom of the cage and moves very little. It died on this evening.

Microscopical examination showed marked hyperæmia and hæmorrhages, but no cellular infiltration. Some of the glia cells distinctly enlarged. The ganglion cells generally dark and rather homogeneous, some of them being besides shrunken and vacuolated, enlarged glia cells often having eaten their way into them; the changes, however, on the whole, not very pronounced.

The clinical picture differs considerably from that which is usually accepted as that of poliomyelitis, as do also the pathological findings. The question might well be asked, Is this disease poliomyelitis?

Flexner, Clark and Fraser [58] are unwilling to accept these pathological findings as evidence of poliomyelitis because similar lesions have

not been shown to be present in fatal cases of poliomyelitis in man and because the organs of monkeys showing such lesions were only occasionally reinoculable and did not cause in the second generation in monkeys characteristic histological effects.

(9) *Pathological Changes found in Experimental Poliomyelitis.*

Most observers agree that the histological changes characteristic of epidemic poliomyelitis are similar in man and monkey. The lesions consist of necrosis and degeneration of the ganglionic nerve cells, with œdema, hæmorrhage, and leucocytic infiltration of the ground substance, the sheaths of the blood-vessels and the membranes.

Wickman believes that the virus produces both interstitial and parenchymatous lesions; Leiner and Wiesner think the virus attacks the parenchyma of the nervous system primarily, and the interstitial changes are secondary.

Flexner, from his histological study of spinal cords in the pre-paralytic stage of the experimental disease, shows the important fact that the interstitial changes are well advanced while the nerve-cells present a normal appearance. He points out the almost constant infection of the intervertebral ganglia in both human and experimental infection by inter-cellular invasion from the periphery to the centre, and comes to the conclusion that the virus acts chiefly upon the interstitial element of the meninges, causing a cellular, chiefly lymphocytic, accumulation, most abundant about the blood-vessels through which various parenchymatous cells become injured and destroyed.

Kling, Pettersson and Wernstedt [64], from their extensive series of experiments, describe two distinct pathological conditions in the monkeys dead of poliomyelitis: the one interstitial, the other parenchymatous:—

(1) The infiltrative type, the pathological picture commonly presented by the spinal cord of monkeys in connexion with experimental poliomyelitis.

(2) The degenerative type, in which cellular infiltration is absent and the striking change is degeneration of the nerve-cells. This degeneration affects not only the nerve-cells, but also the cells of the glia. The authors describe, in fact, two degenerative types: *the one* in which the ganglion cells are encroached upon by a large number of cells which are polymorphonuclear leucocytes and polyblasts, the polyblasts being, according to Wickman, the real neuronophages; *the second*, in which a cell having a large, clear, rounded cell-body eats its

way into the ganglion cell. This the authors designate as "glia-cell neuronophagia."

An important point is the proportion between the cases in which infiltrative and degenerative changes have been observed in experimental animals.

The figures show that animals inoculated from virulent cases give a far greater percentage of infiltrative cases than those inoculated from abortive and convalescent cases:—

	Animals dead	Infiltrative	Degenerative
(1) Typical cases	59 ..	25 (42 per cent.) ..	34 (58 per cent.).
(2) Abortive and virus carriers ..	34 ..	1 (3 ") ..	33 (97 ").
(3) Convalescents.. .. .	23 ..	2 (8 ") ..	21 (91 ").

The greater virulence and the appearance of the inflammatory infiltration evidently go hand in hand in the monkey. The authors come to the conclusion that the degeneration of the ganglion cells, as well as the cellular and humoral exudation, are to be regarded as the result of a direct injurious influence of the virus. This is a new light in which to regard the action of the virus of poliomyelitis, for in the past the changes in the nerve-elements have been regarded as secondary to the infiltration of the tissues. Further experiments are necessary to confirm or disprove the view expressed by these authors.

The view held by most experimenters is that the changes found in the brain and spinal cord in experimental poliomyelitis do not differ from those found in natural infection. In the spinal cord the lesions are usually more severe and widespread than in the brain. The meninges usually show a more or less diffuse infiltration with round cells. The layers immediately next to the white matter of the cord tend to show more cells than the layers next the dura mater. The greatest accumulation of cells is about the arteries and veins, the sheaths of which are surrounded by cells. The effect of these cells on the lumina of the smaller vessels is considerable. The meningeal cellular invasion is only interstitial, and does not give rise to an exudate upon the surface of the cord or brain such as occurs in acute exudative inflammation.

In concluding this digest of the experimental work, I have endeavoured to put before you the present view of the subject taken by the American and Continental schools. Many questions have been answered, but there are others which are still debatable, and one of the most important is that raised by the clinical and pathological picture produced by Kling, Pettersson and Wernstedt as the result

of these injections. Should their work be established, it will give to poliomyelitis an even wider clinical and pathological aspect than it has acquired during the last decade.

CHAPTER IV.—“POLIOMYELITIS” IN ANIMALS.

Infection of Animals other than Monkeys and Apes.

Most observers have failed to transmit human poliomyelitis to animals other than monkeys and apes. Flexner and Lewis tried the horse, ox, pig, rat, cat, and rabbit; Levaditi and Landsteiner tried the rabbit, guinea-pig, young dogs, and sheep. Leiner and Wiesner tried young dogs, fowls, pigeons, and rabbits; and Roemer rabbits, guinea-pigs, and mice—all without success [70].

Krause and Meinicke, Lentz and Huntemüller assert that they transmitted poliomyelitis regularly to rabbits. These rabbits succumbed with or without paralytic symptoms, and on histological examination the characteristic changes of poliomyelitis, more or less pronounced, were found. These investigators think that the inoculation into rabbits of cerebrospinal fluid, blood, brain, or spleen obtained from human cases of poliomyelitis leads to the death of these animals, and the inoculation of similar tissues obtained from rabbits that have succumbed into other rabbits will bring about their death. When the injections were made into the blood and peritoneal cavity a greater number of positive results were obtained than when they were made into the brain. The effects could be produced in rabbits, not only with an emulsion of the organs mentioned, but also with Berkefeld filtrates prepared from them. Levaditi once succeeded in transmitting poliomyelitis to a rabbit, and the spinal lesion was even more marked than in a monkey.

Marks [78] has further investigated this question. He used young rabbits; these were injected with an emulsion of the spinal cord from a poliomyelitic monkey; 2·5 c.c. to 3·5 c.c. of the emulsion was injected intravenously and intraperitoneally. The injection had no immediate effect on the rabbit. Some of the animals injected died between the eighth and fifteenth days after injection. When death occurred the symptoms came on suddenly, the final stage being generally ushered in by convulsions and rigidity, and death took place in from ten to thirty minutes after the onset of the symptoms. The post-mortem examination showed hyperæmia of the cortex, but no other striking lesion; and microscopical examination failed to show any further characteristic change. Other rabbits were injected with emulsions from various

organs of the rabbits which died, and some of these rabbits succumbed. The virus was thus passed through a series of six rabbits. From rabbits in the second, fourth and sixth set of the series of rabbits, monkeys were inoculated, and these monkeys all developed typical poliomyelitis.

These results leave no doubt that poliomyelitis can be propagated in certain individual rabbits, and that the virus is not confined to the central nervous system, but occurs in equal amount in other organs. It is probable also that not all strains of the virus can be transmitted to even a small fraction of individual rabbits, and this may account for Roemer and Joseph's failure in a long series. It is thus established that the virus of poliomyelitis can survive and probably be propagated in domestic animals that do not show any of the symptoms of poliomyelitis as it occurs in man.

Roemer [70], who has carried out a large series of experiments on rabbits, does not believe that they are a suitable animal for the investigation of poliomyelitis. He says thirty-one rabbits in four series received large doses of material containing the virus of poliomyelitis by simultaneous intravenous and intraperitoneal injection. The virulence of the material used was proved by the fate of the four control monkeys, which all died of typical poliomyelitis.

Of the thirty-one rabbits, thirty remained well for four months under daily observation, one animal suffered from an atypical form of paralysis, for which no lesion of the nature of poliomyelitis could be made responsible.

The similarity of the virus and of the pathological lesion of poliomyelitis and that of rabies, a disease of which the carrier species is known to be canine, suggest the possibility of some similar animal carrier for poliomyelitis. It is therefore important to investigate the paralyzes of animals occurring at the same time as poliomyelitis in man, or of cases in animals presenting similar clinical features or pathological appearances. The simultaneous occurrence of paralysis in fowls and poliomyelitis in man has been noted by Krause, and he refers to other observations of the like nature. He failed to find any pathological lesion in the fowls investigated.

Lust and Rosenberg [74] carried out a series of experiments endeavouring to infect fowls, but they were unable to infect them either naturally or experimentally.

C. S. Shore, veterinary surgeon, refers to a disease appearing in one to two-year-old colts that showed a line of symptoms closely resembling poliomyelitis in children.

Reece, in his report on the epidemic of poliomyelitis in Devonshire, referred to the affection of pigs, to poke-neck in horses, to an affection of fowls, and to the death of a bull and a calf. No pathological examination was made in these cases. He also refers to a large mortality in Sweden of reindeer, poultry, and dogs from a disease stated to be poliomyelitis.

Roemer [79], in 1911, described a disease like poliomyelitis which arose spontaneously in guinea-pigs. The disease was due to an ultra-microscopic organism, which could withstand the action of glycerine and could be transmitted from guinea-pig to guinea-pig by intra-cerebral injections. Monkeys were not, however, susceptible to the disease, and though in its characteristics it closely resembled poliomyelitis, yet it is clear that it is distinct from that disease.

McGowan and Rettie [76] described poliomyelitis in sheep suffering from "loupin ill" and changes in the central nervous system similar to those found in poliomyelitis, but they were not able to transmit the disease by inoculation.

Holmes and myself [71], 1908, have described perivascular lymphocytosis and changes in the central nervous system of a dog which suffered from paralysis, and in 1913 Flexner and Clark [73] described paralysis in a dog simulating poliomyelitis. They were not, however, able to transmit the disease to other dogs by intraspinal inoculation.

Borna disease in horses, again, has a similarity, both clinically and pathologically, to poliomyelitis.

Marchant and Petit [77] describe a case of acute poliomyelitis with symptoms like Landry's disease in a mare. The animal died on the seventh day of illness, and the spinal cord showed foci of inflammation and degeneration of the ganglion cells. No micro-organisms were found. A guinea-pig inoculated with the blood of the mare died on the third day, but the examination showed nothing definite.

McGowan and Dawson [75] compare the lesion of the nervous system in distemper of the dog with those of human poliomyelitis, and come to the conclusion that they are strikingly similar.

The failure to communicate the diseases to monkeys, and in some cases even to animals of their own species, makes it almost certain that the diseases described in animals are distinct from poliomyelitis of man, though bearing some resemblance both clinically and pathologically.

Bruno [72] brought forward evidence of infection from ducks, and the simultaneous appearance of paralysis in a cow and goat.

The relationship of the diseases in animals to those in man is a question which needs most careful investigation.

CHAPTER V.—SERUM DIAGNOSIS.

(1) *Experimental method*.—Levaditi and Landsteiner and Müller have shown that it is possible to test the serum of patients and monkeys for their viricidal properties. For this purpose a 5 per cent. emulsion of the spinal cord containing the active virus is mixed with an equal quantity of the serum to be tested. The mixture must be made at a temperature of 34° C., and stood at room temperature for several hours. It is then injected intra-cerebrally in quantities of 0·6 c.c. to 0·8 c.c. into a normal monkey. A control monkey receives the same quantity of the virus. The control monkey becomes infected, the other monkey remains free. This experiment has been tried with the blood of a patient who has had herpes zoster, but the experiment was inconclusive, as the control monkey was not affected (Müller).

Anderson and Frost found that the blood serum, in six out of nine suspected cases of abortive poliomyelitis, was viricidal against the virus of the poliomyelitis. Landsteiner, Levaditi, Leiner and Wiesner have all shown that the serum is viricidal *in vitro*, but not *in vivo*. The serum injected into animals has no preventive or curative effect. The sera of animals has no viricidal power.

(2) *Fixation of the complement method*.—This point has been investigated by Wollstein, Roemer, Joseph, Levaditi and Landsteiner. All these observers agree that the use of an extract of organs containing the virus as antigen does not permit the discovery of antibodies in the serum or cerebrospinal fluid.

Roemer and Joseph call attention to the fact that this absence of amboceptor is similar to that in rabies, for no amboceptor has been demonstrated in that disease.

Peabody, Draper and Dochez carried out a series of tests with blood sera from—(1) normal persons; (2) from those exposed to infection in the ward or suspected abortive cases; (3) from typical cases, the serum from the patients being mixed with a known dose of the active virus incubated for one to two hours at 37° C., and allowed to stand in ice for twenty-four hours. The injections were then made intra-cerebrally into monkeys. The result was that the sera of the typical cases protected the monkey, but the sera from the normal and abortive cases gave uncertain results. So far no serum test, other than the above, has been devised. Such a test would be of the greatest value, for it would serve to render clear the nature of many cases of certain nervous diseases in children, the cause of which at the present time remain obscure.

CHAPTER VI.—CLINICAL FEATURES.

(1) *Forms of Poliomyelitis.*

Recognizing that poliomyelitis is an acute infective disease which may attack any portion of the nervous system, it is at once apparent that the clinical picture may be most varied according to the situation of the lesion. Many observers have collected and tabulated their cases according to the part of the body paralysed, and it has been shown that the legs, and especially the distal muscles, are more commonly affected than any other part. Isolated paralysis of the trunk muscles occurs in about 1 per cent., and isolated paralysis of the cranial nerves in about 2·5 per cent. Wickman's figures show that in 68 per cent. of all cases the legs are affected. Wickman divided the cases into various groups on an anatomical basis, according to the portion of the nervous system involved. The groups are as follows :—

- (i) The spinal form.
- (ii) The bulbar, pontine and mid-brain form.
- (iii) The cerebral form.
- (iv) The cerebellar form.
- (v) The meningitic form.
- (vi) The neuritic form.
- (vii) The abortive form.

Peabody, Draper and Dochez [107], in their excellent monograph on the clinical features of poliomyelitis, criticize this classification, saying that it is based neither on pathological anatomy nor on clinical symptomatology, but on a mixture of the two. They prefer the classification suggested by Müller on an anatomical basis—viz. :—

- (i) Spinal form.
- (ii) Bulbar form.
- (iii) Cerebral form.
- (iv) Abortive cases.

But even here a clinical type (abortive cases) has to be introduced to complete the classification. No other classification seems to me to be so helpful in the clinical description of the disease as that given by Wickman.

(i) *The Spinal Form.*

This is the common manifestation of the disease, and the type most usually seen is that of a flaccid paralysis of one or more limbs; sometimes all the muscles of both limbs, trunk and neck are completely paralysed. The clinical variations in this form are, however,

considerable and require special notice, for they are not always recognized as manifestations of poliomyelitis.

Ascending and descending type: A type which is not common, and is more frequently seen in adult life than in childhood, is the ascending type (sometimes called Landry type), in which the disease, starting from below, gradually ascends and affects successively the legs,



FIG. 24.—Photo of a boy with paralysis of the intercostal and abdominal muscles and complete collapse of the right lung due to poliomyelitis. The heart is displaced to the right side, as indicated by the shaded area on the chest wall.



FIG. 25.—Lateral view of same case, showing the prominence of the abdomen due to weakness of the abdominal muscles.

the abdomen, the thorax, the arm and neck, so that eventually the respiratory centres are involved and the patient dies from failure of respiration, consciousness often being retained to the end.

This ascending progress of the disease is not always uniform; the disease after affecting the lower limbs, will sometimes cease, and then, after an interval of two to three days or it may be even ten to fourteen,

again start its upward course, possibly again become arrested for a time, and then make further progress until the respiratory centre or the bulb becomes involved. These have been designated the "jump" cases, and experimentally similar manifestations have been noted by Roemer in the monkey [50], and he refers to a similar instance reported by Levaditi and Stanesco.

Sometimes the disease will manifest itself first in the upper segments of the cord, and involve the lower limbs at a later period (descending type).

Thoracic and abdominal type: Sometimes the disease will involve the thoracic and abdominal muscles alone, leaving the limbs unaffected, and in such a case the acute respiratory disturbance suggests the onset of pneumonia. This is intensified when accompanied by complete collapse of one lung. It is difficult to say whether the collapse of the lung occurs at the same time as the paralysis of the intercostal muscles or is due to the blocking of the bronchus by mucus which there is no expiratory effort to expel.

The following case illustrates this condition (fig. 24):—

A. H., aged 4, taken ill in August, 1914, with "pneumonia." Six weeks later he was admitted to the hospital with complete paralysis of the intercostal and upper abdominal muscles, but without any marked affection of the limbs. He had complete collapse of the right lung, and the heart was displaced to the right side. Endeavours were made to expand the right lung without success, and eighteen months later the condition of the lung was unaltered, and the heart in the same position. Respiration is carried on entirely by the diaphragm.

Sutherland [113] has described a similar case in an infant, aged 15 months, with paralysis of the abdominal muscles and collapse of the right lung.

Abdominal muscles: Paralysis of the abdominal muscles frequently accompanies that of the intercostals. The weakness of these muscles gives rise to difficulty in rising from the lying into the sitting position, and to a marked prominence when the patient assumes the erect position (fig. 25). During inspiration it is not unusual to see marked recession of the epigastrium. It is not uncommon to see a partial paralysis of the abdominal muscle, so that when the child coughs or strains there is a protrusion of the abdominal contents into the thinned abdominal parietes, and such a protrusion suggests to the parent that a tumour is growing in the abdomen (fig. 26). Although paralysis of the abdominal wall most frequently occurs in association with thoracic and limb paralysis,

yet it may be absolutely limited to a small portion of the abdominal or oblique muscles, and be the only manifestation of a past poliomyelitis.

Weakness and paralysis of the dorsal muscles of the back prevent the child from assuming the erect position either when sitting or standing. The trunk falls forward and the child is unable to erect it. Such a weakness often gives rise to the saddle-back and to the quadruped walking



FIG. 26.—Photo of girl, showing local bulging of the abdominal wall due to poliomyelitis. (For this photograph I am indebted to Dr. Sutherland.)

adopted by these children as a mode of progress (fig. 27). It is the weakness of these muscles which gives rise to the most marked lateral curvatures.

Transverse lesion: A somewhat rare manifestation of acute poliomyelitis is a transverse lesion of the spinal cord, so that the patient has complete flaccid paralysis of both legs, loss of sphincter control, and loss of sensation to the level of the lesion. This lesion may remain complete, or may clear up, leaving the patient with spastic paraplegia

with increased knee-jerk, ankle clonus, and defective control over the bladder. As illustrative examples the following cases may be quoted:—

F. T., aged 19, was taken ill January, 1914, with fever and pains, and with a rapidly progressive paraplegia which became complete in forty-eight hours, giving rise to an absolutely flaccid paralysis of both legs with loss of sensation to a line 1 in. above the umbilicus. There were retention of urine and an absence of all the deep reflexes. About six weeks later the knee-jerk returned, and eventually both legs became spastic. Sensation also began to return. The examination of the blood and cerebrospinal fluid excluded syphilis. The possi-



FIG. 27.—Boy with extensive poliomyelitis, especially of the extensors of the thighs on the trunk. He was unable to maintain the erect position, and adopted the quadruped method of walking.

bility of an extradural hæmorrhage and tumour was excluded by operation, which revealed a cord presenting almost a normal appearance. The girl, after eighteen months, recovered some power in the legs, but was left in a very spastic condition.

J. D., aged 6, was taken ill on May 2, 1915, with convulsions, fever, pains in the back, and weakness of both legs and arms. The sphincters were affected. He was admitted to hospital August 6, 1915. He had then a very spastic condition of both legs, with considerable adductor spasms and very little power of movement. The knee-jerks were increased, there was ankle clonus on both sides, and the plantars were extensor. No alteration in sensation could be detected. The cerebrospinal fluid was normal, and both blood and cerebrospinal fluid gave a negative Wassermann. The X-rays

showed there was no disease of the vertebræ. On August 14 he developed measles, and during his convalescence therefrom the power in his legs began to improve, the improvement being maintained, so that when he left the hospital on October 25 he could walk fairly well, but was still spastic.

When the lesion is situated in the cervical region, weakness and wasting of the hand and arm muscles, and a spastic condition of the leg, may occur:—

E. D., aged 2, was taken ill in July, 1913, with a rise of temperature, profuse sweating and great pain and screaming attack; his illness was attributed to a circumcision which had recently been performed. After recovering from the acute attack, which lasted about seventeen days, it was noticed that he could not move his hands, and was very weak in the legs and back; it was also noticed that his knee-jerks were brisk and ankle clonus was present. When seen in October, 1913, there were marked weakness and wasting of the small muscles of both hands, drooping of the eyelid (probably due to sympathetic affection), a spastic condition of both legs with increased knee-jerks, ankle clonus and extensor responses; no sensory defect. The X-rays showed no disease of the cervical vertebræ. The boy slowly improved, but two and half years later still had marked weakness of the small muscles of the hand and a spastic condition of the lower limbs.

It is admittedly difficult in the cases like those above quoted to give positive proof that the lesions were due to the virus of poliomyelitis, for such cases rarely die, so that pathological and experimental evidence is wanting. It has not been possible to carry out the serum test. But by excluding the common causes of transverse lesion one is justified in suggesting that poliomyelitis may be the causal factor.

B. Sachs [110] records a case of acute poliomyelitis in a girl, aged 18, with sudden onset of complete flaccid paralysis and loss of sensation to the xiphoid with complete recovery in two months. The cerebrospinal fluid showed a high lymphocytic count.

Netter and Levaditi [103] report four cases presenting symptoms of transverse myelitis which they attribute to the virus of poliomyelitis. They were able to show that the blood of a patient who had recovered possessed the properties for neutralizing the virus of poliomyelitis.

Strümpell [112] records a case in a man, aged 19, of sudden onset of paralysis of the arms with considerable loss of sensation in the trunk and leg below the seat of the lesion. This lesion he attributes to poliomyelitis. Similar observations have been made by others.

Abnormal attitudes assumed in incomplete paralysis: When all the muscles of a limb are involved a complete flaccid palsy results, and no abnormal attitude is assumed or deformity produced; but in many

instances certain groups only are involved, and the contraction of the unbalanced antagonistic muscles gives rise to unusual position and deformities. The two following cases illustrate this point. They must, however, be considered rather unusual manifestations of the disease. The first is that of a child in whom the extensors of the right thigh were completely paralysed, whilst the flexors were unaffected, the result being that the leg was held erect in the air as the child lay in bed (fig. 28).

In the less extreme examples of this form the leg is held out in front, and gives rise to a difficulty in walking quite out of proportion



FIG. 28.—Infant with poliomyelitis of both legs and arms, the right leg is held erect in the air owing to the paralysis of the extensors of the thigh and the unbalanced contraction of the flexors. The leg is being steadied by the hand of an observer for photographic purposes.

to the weakness of the limb, and the attempt to bring it into line with the trunk only produces a lordosis, or the trunk is bent forward with a loss of balance. When this deformity is bilateral the lordosis becomes marked, and the child can only assume the erect position by an extreme lordosis of the spine (fig. 29).

The reverse of the above condition is seen in the case of a child in whom the flexors of the thigh are paralysed, whilst the extensors are unparalysed and in active contraction. Such a condition gives rise to a rigid child, the legs cannot be flexed and the child can be supported by the head and heels, and held out in a rigid position such as shown in fig. 30. The case is as follows:—



FIG. 29.—Girl with extensive poliomyelitis and bilateral contraction of the flexors of the hip-joints.
In the attempt to assume the erect position a lordosis of the spine is produced.



FIG. 30.—Child with extensive poliomyelitis, showing rigid extension of the hips, due to the unbalanced action of the gluteal muscles. This rigidity was such that the child could be supported by one hand placed under the head, and the other under the heels.

Poliomyelitis with rigid extension of the legs at the hips: H. G., the fifth child of a family of five, was taken acutely ill with poliomyelitis in September, 1912, the limbs, trunk, face and eyes being affected at the onset. He was acutely ill for fourteen days, then gradually recovered the power in his right arm, but had severe pain and tenderness in trunk and lower limbs. When seen in March, 1913, both legs were rigid at the hips and everted, and attempts at movement caused acute pain. Below the knee the muscles were flaccid and the feet in a position of equinus. The shoulder muscles of the left arm were completely paralysed, and there was likewise considerable intercostal and abdominal paralysis. The child was quite rigid in the extended position, and if lifted off the bed by one hand placed under the head and another under the heels, he maintained this extended position (fig. 30). This rigid extension of the hips appeared to be due to the unbalanced action of the gluteal muscles, the psoas and the iliacus muscles being completely paralysed. Any attempt at flexion of the hip gave rise to pain, but if once flexed, the hip-joint could be moved in any direction quite easily. X-ray examination made it certain that there was no hip disease. All the deep reflexes were abolished in the lower limbs. The pain on movement in this case persisted for over fourteen months. In this case the child was up in plaster of Paris in a position of flexion, so as to overcome the extension and allow the flexors to recover. Although the child was kept for months in this position, yet he always, in a few days after the plaster was removed, reverted to the rigid extended position. It is interesting to note that when first taken out of plaster the legs remained in the flexed condition for a few hours. Massage, movements, hot baths, had no effect, either in overcoming the rigidity or of removing the pain on movement.

Paralysis of neck muscles: In some cases the neck muscles may alone be affected, so that the head flops about in all directions. In one case the affection was almost limited to the neck muscles, the shoulder muscles being but slightly affected, whilst the muscles supplied by the bulb escaped entirely; the diaphragm, too, was unaffected (fig. 31):—

William F., aged 11, was taken acutely ill in March, 1915. He had severe headache, vomiting and constitutional symptoms; one week after onset a measles-like rash appeared which lasted two days. He had, when seen ten days after the onset, some weakness of shoulder muscles and complete flaccid paralysis of the neck muscles, being quite unable to hold the head up. He at no time had any bulbar symptoms. He could move the arm well and had full power in the thoracic, abdominal, and leg muscles. He was quite unable to sit up or walk, owing to the weakness of his neck muscles. The cerebrospinal fluid was clear, contained 0.15 per cent. albumin, no cells, and gave a negative Wassermann reaction. The neck was splinted (*see* fig. 43), and the boy gradually recovered power, but considerable weakness of sterno-

mastoid and trapezius remained. He could walk quite well as long as his head was supported by the splint.

Unilateral paralysis of the diaphragm: The diaphragm may be affected at the same time as the intercostal muscles, and sometimes one



FIG. 31.—Boy with complete flaccid paralysis of neck muscles, those supplied by the bulb escaped entirely (compare fig. 43), and the limb muscles almost entirely.



FIG. 32.—Unilateral paralysis of the right side of the diaphragm (from an X-ray kindly lent by Dr. Voelcker).

side of the diaphragm is involved whilst the other moves well. This is best seen on an X-ray screen, when the movements can be watched (fig. 32).

Sympathetic paralysis : Paralysis of the sympathetic fibres has been noted in cases of poliomyelitis in the region of the first dorsal and lower cervical segments of the cords, but no observations have been made on the occurrence of subnormal temperature such as is known to occur and has recently been noted by Gordon Holmes in the Goulstonian Lectures in injury to the lower cervical region of the spinal cord.



FIG. 33.—Paralysis of the right side of the face, associated with flaccid paralysis of the muscles of the right shoulder.

(ii) *The Bulbar, Pontine and Mid-brain Form.*

Bremer [85], in an analysis of 400 cases of poliomyelitis from the records of the Children's Hospital, found that forty-eight—i.e., 12 per cent.—showed some evidence of an encephalitis, facial paralysis being the commonest manifestation, whilst ataxia, nystagmus and tremor formed the next most numerous group. The clinical manifestations exhibited by lesions in this region are most varied. Any extensive lesion in the bulb is almost always rapidly fatal, and a typical instance of such with a good pathological examination is recorded by Feiling [90].

The acute symptoms may be severe, yet they will often clear up, leaving a paralysis limited to one or more cranial nerves.

Lesions in this region may affect any one or more of the cranial nerves; that which is most commonly attacked is the seventh, giving rise to a facial paralysis of the lower motor neuron type (fig. 33). When such a paralysis is associated with a poliomyelitic lesion in the cord, causing a limb paralysis, or when another member of the family is affected with the ordinary type of poliomyelitis at the same time, it is not difficult to recognize the nature of the affection; but when the facial paralysis occurs as the solitary manifestation, considerable difficulty arises in regard to the diagnosis. It has been noted that the number of cases of facial paralysis among children tends to increase with the prevalence of poliomyelitis.

Of the other cranial nerve nuclei, those supplying the tongue, the palate, the masseter and temporal muscles may be affected, either unilaterally or bilaterally. The oculo-motor nuclei may be affected, giving rise to a complete or partial ophthalmoplegia. Blindness is sometimes associated with the paralysis. Return of vision and complete restoration of power in the muscles may take place, or the ocular palsy may clear up, leaving the child completely blind. I have recorded such an association in a child:—

M. S., aged 5½, taken ill acutely with headache, followed by loss of sight and complete ophthalmoplegia externa; the ophthalmoplegia cleared up almost entirely in a month, leaving the child, however, completely blind. There was slight swelling of the disk, but not a marked optic neuritis.

That poliomyelitis may, in some cases, account for the sudden loss of vision and of hearing is possible, but pathological confirmation has not been obtained.

Associated myelitis and optic neuritis: E. Clowes [86] records a case of acute myelitis with optic neuritis in which the sudden onset, the character and progressive nature of the symptoms, with death on the fourteenth day of illness, strongly suggest the possibility of poliomyelitis as the causative factor. Unfortunately no pathological examination was obtained.

Dr. Frederick Taylor [114] alludes to the association of optic neuritis with spinal lesion, of which there are a number of recorded instances. Many of these cannot be attributed to poliomyelitis. It is, however, the acute and sudden onset of both spinal and ocular symptoms which is the feature which so strongly suggests the poliomyelitic infection.

Hertz, Johnson and Depree [96] record the case of a boy, aged 12½,

who had acute onset of paralysis with optic neuritis and ocular palsy. The cerebrospinal fluid showed lymphocytosis and polymorphonuclear cells in almost equal numbers. The boy recovered to a very considerable extent. The authors regard this as a case of polio-encephalo-myelitis.

Mid-brain lesions: The symptom most characteristic of lesions in mid-brain is that of a rhythmic tremor of the limbs associated with an ocular and sometimes other cranial nerve paralyses. Holmes has described the tremor of mid-brain lesion as a slow regular tremor, increased by involuntary movement and by excitement. It may be universal and affect the whole body, but in most cases is limited to the limbs and is seen in its most typical form in the arms. There is an increase of tone and some disability in using the limb, but there is no true spasticity, and the limb is in a condition of "plastic tone." As illustrative of this condition the following case, recorded by Leonard Parsons [106], may be quoted:—

A girl, aged 2, was at play and apparently quite well on the evening of July 15. She was put to bed and noticed to be feverish. At 10 p.m. she had a fit, became sleepy and unconscious. At 10 a.m. and 12 noon she had a recurrence of the fits. On recovering consciousness it was noticed that she was trembling all over; the tremor affected the tongue, arms, legs and trunk, and was exactly like shivering. For three weeks she remained in bed, during which time the tremor persisted; she was apparently conscious, took her milk, but her eyes were fixed and staring and she did not appear to see anything, nor did she speak. When admitted to hospital on August 2, there was slight retraction of the head, her expression was staring and she was apparently quite blind. There was present a slow, rhythmic tremor of the arms with marked rigidity of the limbs, but no evidence of paresis. The knee-jerk and abdominal reflex were present, and the plantar responses were flexor. Both pupils reacted to light, and the fundi showed no change. There was broncho-pneumonia. The cerebrospinal fluid was examined and no lymphocytosis or organisms were found. On August 24 the child spoke for the first time, and it was noticed that her vision had returned. On September 4 the tremor was no longer present whilst the child was at rest, but was brought out by voluntary movement. She left the hospital on September 12, but she still had some tremor on voluntary movement. She was seen again in February, 1910, when she appeared well and talked freely.

Other cases occur in which ocular palsy and nystagmus are present, and others again in which there is evidence of involvement of the fifth, sixth and seventh cranial nerves, the variation in symptoms depending on the situation and extent of the lesion.

It may be well to mention here the movements which Netter and Ribadeau-Dumas [104] describe as chorea occurring before and during

the onset of acute poliomyelitis, and these are probably of the same nature as those described by Colliver [87] under the name "A pre-paralytic symptom in acute poliomyelitis" as a tremor and convulsion of certain groups of muscles.

(iii) *Cerebral Form.*

The most characteristic feature of this type is hemiplegia. The onset of the illness is sudden, associated with convulsions, which may be unilateral or bilateral, and loss of consciousness, and the child, on recovery, is found to be hemiplegic. Poliomyelitis is probably not a frequent cause of infantile hemiplegia. Of 100 cases of infantile hemiplegia collected by myself, only ten could on clinical grounds alone be ascribed to polio-encephalitis, the criteria for such being that the child was perfectly healthy before the onset, the onset was sudden, that it occurred during the summer months, and the symptoms were retrogressive after the attack was over, and that there was no cardiac or other condition likely to give rise to a hemiplegia.

Should the hemiplegia be associated with a poliomyelitis of the limbs, it may with reasonable probability be assumed that the lesions are due to the same causal organisms, and a striking instance of such an association has been published by Rossi [109], the diagnosis being verified by a pathological examination, to which allusion has already been made in the section dealing with pathology.

An American writer, Manning [99], tries to prove that the attack of hemiplegia from which Pasteur suffered at the age of 46 was due to a poliomyelitis—the infection being derived from the silkworm, Pasteur being engaged on that work at the time.

Athetosis of left arm and left side of face, flaccid paralysis of left leg, and some flaccid paralysis of right leg: The association of a hemiplegia with athetosis with a poliomyelitis is one of the rarest manifestations of the disease, and the following instance may be given:—

A. A., aged 7, was the seventh of eight children. She was a healthy baby till the age of 10 months, when she had an acute illness with convulsions. From this she recovered, but it left her with paralysis of the left side. She subsequently learnt to talk, was intelligent, and went to a school for physically deficient children. She never learnt to walk. When first seen she was a pale child, with marked athetosis of the left arm and involuntary movements of the left side of the face. She was unable to stand, and if an attempt were made to place her on her legs, she supported her weight on the right leg with the knee flexed, the left leg being too weak to support any weight. The left hand exhibited spontaneous movements of an athetoid character (fig. 34),

which were increased on attempting to walk or on any emotional stimulus. The child had little voluntary power of movement in the left hand; there was, however, no rigidity, and the hand, though at times strongly contracted, yet when moved passively was quite flaccid. The left leg showed the typical flaccid palsy of poliomyelitis with wasting of muscles, loss of deep reflexes, and loss of electrical reaction of all muscles below the knee, and to a lesser degree above the knee.



FIG. 34.—Athetosis of the left arm and left side of the face, associated with a flaccid paralysis of the left leg, and partial paralysis of the right leg.

This case illustrates the association of an athetosis with a poliomyelitis. There is no reason to doubt that the paralysis of the legs is due to a spinal lesion, and the athetosis of arm and face to a cerebral lesion. It may be questioned whether there is sufficient evidence to prove that the condition is the result of the virus of poliomyelitis, but, so far as the legs are concerned, they may be considered typical of the condition. The arm paralysis occurred at the same time, and there

seems no reason for hypothesizing another toxic condition for the production of the focal lesion in the brain. The contraction which was present in the legs has been corrected, and with support the girl walks fairly well. The athetosis of the left arm persists.

Mental defect: Cases in which marked mental defect persists after an acute cerebral attack in children are not uncommon, but the difficulty of proving that such cases are due to poliomyelitic virus is considerable. Such cases may or may not be accompanied by an alteration in the cerebrospinal fluid. When accompanied by a lympho-



FIG. 35.—Child with acute cerebellar ataxia attempting to walk. The nurse is preventing the child from falling backwards, a tendency which such cases commonly exhibit. Note the wide base and the spread arms.

cytosis the cases come within the meningeal group and are dealt with under that head, but those cases in which the fluid is perfectly normal correspond closely to those in which the poliomyelitic virus affects other portions of the brain and spinal cord, no change being found in the cerebrospinal fluid.

The cases of this type have always been isolated, and I have never seen this form in one member of a family in which others have typical poliomyelitis. Pathological proof of the nature of the affection has not been obtained.

(iv) *The Cerebellar or Ataxic Form.*

This type is characterized by the acute onset of ataxia, sometimes associated with ocular and other cranial nerve paralyses and alteration of articulation. Nystagmus is often absent. As with other forms of poliomyelitis, the onset may be attended by malaise and vomiting, but in other cases the onset is quite sudden, and the child having gone to bed perfectly well, is found in the morning to be wildly ataxic, but otherwise not ill. In some cases the ataxia clears up rapidly, so that after ten to fourteen days the child is quite well. In other cases it takes many months and sometimes years to clear up.

An interesting instance of slow and gradual recovery in a boy who, after an acute illness, was ataxic for some three years has been recorded by Dr. Frederick Taylor [115]. When seen some twenty-five years later he was in every respect a normal individual, and had been so during boyhood and manhood, having played the usual games necessitating good co-ordination.

The following is an instance of one child in the family being affected with the ordinary type of poliomyelitis and another with ataxia:—

Poliomyelitis and ataxia: probably due to involvement of the cerebellum: R. S., aged $5\frac{1}{2}$, and M. S., aged $1\frac{1}{2}$, are brother and sister, and they were both taken acutely ill within a week of one another on August 16, 1909. The elder child had left facial paralysis and ataxia of the right arm and leg, whilst his sister had paralysis of the left side of the face and flaccid palsy of the neck muscles. In the elder child the ataxia cleared up in about fourteen days after the onset of the acute illness. The paralysis of the face cleared up somewhat later. In the case of his younger sister the weakness of the face persisted for many months, as did also the weakness of the muscles of the neck, some permanent paresis of the neck muscles remaining. In these two cases there is no doubt that the paralysis was due to acute poliomyelitis, and in the case of the older child it seems probable that there was a focus of the disease in the cerebellum.

Numerous other instances of acute cerebellar ataxia might be quoted, some of which have cleared up rapidly, and others have persisted for months and years.

In those cases in which ataxia of sudden onset is the only symptom it may well be doubted if they are caused by poliomyelitic virus, but the same cannot be said of those cases in which the ataxia is seen in conjunction with other more usual manifestations of the disease, or in such cases as those in which one member of the family has definite poliomyelitis and another is affected with ataxia.

That the lesion is in the cerebellum also may be questioned, for there is but little pathological evidence on these cases, but as the clinical signs closely correspond with those seen in definite lesion of the cerebellum, there is little doubt that the lesion lies somewhere in the cerebellar path.

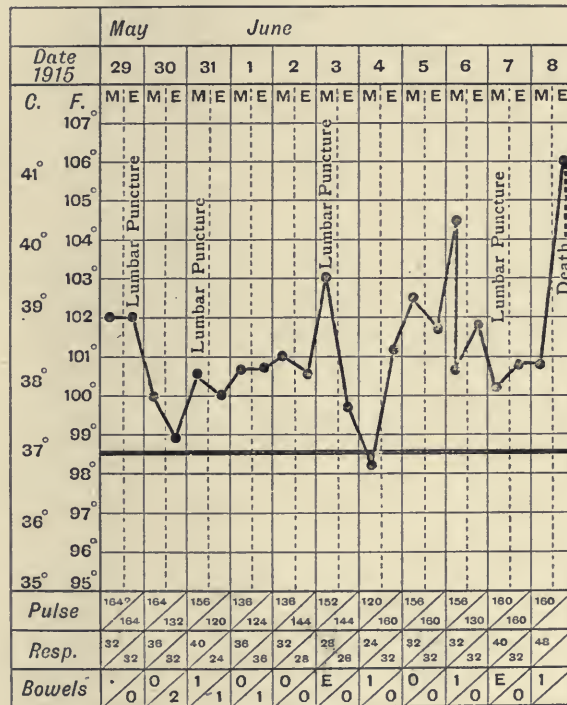
(v) *Meningitic Form.*

Possibly one of the most interesting groups of poliomyelitis, and one which frequently leads to an error in diagnosis, is the meningitic form of the disease. The onset may be sudden, attended by convulsions and coma. This may rapidly pass off, or persist and deepen. Temperature is raised and may remain high for days. The neck is stiff, and the legs rigid in a flexed or extended position, and Kernig's sign may be present. The pulse is slow or rapid, according to the stage of the disease. All the symptoms of a meningitis may be present, and on lumbar puncture the cerebrospinal fluid escapes under pressure, is clear, and on cytological examination may be found to contain an increased number of lymphocytes with a normal, or sometimes a diminished sugar reaction and increased amount of albumin.

The cases thus present the clinical picture and cytological condition of the cerebrospinal fluid which is of frequent occurrence in tuberculous meningitis. If tubercle bacilli are found in the cerebrospinal fluid the diagnosis is clear, but if not found the case falls into the group of lymphocytic meningitis from which recovery is possible. The causes of a lymphocytic meningitis are numerous, and from the examination of the cerebrospinal fluid alone it is not possible to be certain that one is not dealing with a serous meningitis associated with a sinus thrombosis, middle-ear disease, cerebral abscess; with that following mumps or measles; with that due to syphilis or an old and past infective meningitis or to poliomyelitis. As illustrative instances of the meningeal form the following cases may be quoted:—

G. Y., aged 3, was taken ill on June 30, 1913, with sore throat. He was feverish for two or three days. On July 3 he had pains in the back, he cried when moved, and the back was stiff. He was admitted to hospital on July 8 and then had marked retraction of the head and opisthotonos. Any movement of the neck in a forward direction gave rise to pain, but he would allow rotation. There was no rigidity of arms or legs, and the power was good, except in the left leg, which was completely flaccid. On lumbar puncture the cerebrospinal fluid was under pressure, was clear, contained 0.1 per cent. of albumin, no clot, and no cells. The rigidity of the back gradually passed off, but he was left with a flaccid paralysis of the left leg, which recovered to a very great extent after a year's treatment.

R. W. M., aged 5, a patient under the care of my colleague, Dr. Colman. Six weeks previously had measles, from which he rapidly recovered. He came home from school with headache May 26; in the evening he vomited. On the following day he had headache and frequent vomiting. He was feverish. On the morning of May 29 he became convulsed, was delirious, and no longer recognized his mother. He was admitted to hospital, and temperature was 102° F., pulse 164, respiration 32; he was semi-conscious, the neck was rigid, limbs rigid and extended. The cerebrospinal fluid was clear, under increased



Temperature chart of a case of poliomyelitis which presented symptoms similar to those occurring in tuberculous meningitis. Case proved to be poliomyelitis by microscopic examination.

pressure, contained no increase of cells and no albumin, and gave an immediate reduction with Fehling's solution. The condition progressed, the temperature remained high, the cerebrospinal fluid, examined on four occasions, first revealed no cells, then a few, and on the last occasion (June 7) were numerous and were lymphocytic in character; the fluid still reduced Fehling's solution. The boy died on June 8, fourteen days after the onset of the disease. At the autopsy there was no macroscopic meningitis, but on section through the crus and mid-brain marked engorgement of the vessels was found, and on microscopical examination a most extensive perivascular lymphocytosis was present. The spinal cord showed no change.

A third case is that of a boy, aged 4, who six weeks previously had had his tonsils and adenoids removed. He was taken ill on November 16; on November 17 he was feverish, passed into a comatosed condition, was admitted to hospital on the 18th and died on the following day. He was regarded as a case of meningitis, but the lumbar puncture revealed a blood-stained fluid from which it was not possible to make any deduction. *Post-mortem* examination showed extravasation of blood in the region of the cauda equina, possibly due to the lumbar puncture, otherwise the cord appeared to the naked eye normal. On microscopical examination, however, typical poliomyelitic changes were present, most marked in the medulla and in the wall of the fourth ventricle (fig. 18). No change was found in the cerebral hemispheres.

The fourth case is that of a child who presented symptoms of a lymphocytic meningitis with rapid recovery. The details are as follows:—

Betty B., aged 3, the only child of the mother's second family, was taken ill with an attack of vomiting on Friday, September 24, 1915. She was said to have "lost herself" and to have been queer ever since. Her spine seemed to give way and her head was bent to one side. She cried when disturbed and complained of pain at the back of the neck. She was brought to the Hospital for Sick Children, Great Ormond Street, on September 29, 1915, and admitted with the diagnosis of "posterior basic meningitis." On admission, she was a well-nourished child; did not look seriously ill. The temperature was 97° F., pulse 96, and respiration 24 per minute. She sat up in bed of her own accord but held the head towards the right side. On physical examination of the chest and abdomen nothing abnormal could be detected. All movements of the limbs were perfect, but there was slight stiffness of the head and neck and she resented movement. All the deep and superficial reflexes were normal; the optic discs were normal. Kernig's sign was not present. Lumbar puncture was performed and a slightly turbid fluid, just blood-stained, was obtained, which on examination was shown to contain 0·5 per cent of albumin, failed to reduce Fehling's solution, and contained a large number of cells, nearly all of which were mononuclear; no organisms were seen, and the culture on the placenta agar remained sterile; no tubercle bacilli were found. From the examination of the cerebrospinal fluid the most probable diagnosis would seem to be tuberculous meningitis. On October 1 a second lumbar puncture was performed. The fluid again was slightly turbid, formed no clot, gave no immediate reduction of Fehling's solution, contained 0·5 per cent. albumin and a large number of mononuclear cells. No tubercle bacilli were found. On October 8 the child could move the head and neck well and seemed almost normal. Lumbar puncture was performed and the cerebrospinal fluid appeared clear, had no clot, contained 0·125 per cent. albumin, gave no immediate reduction of Fehling, and contained a fair number of mononuclear cells (lymphocytes). Cultures on agar were sterile and on placental agar

anaerobically after three days gave two colonies of *Staphylococcus albus* (contamination). On October 12 the cerebrospinal fluid was again examined; it was clear, the albumin was 0.025 per cent., there was slight immediate reduction of Fehling and was still a *very* slight excess of lymphocytosis; cultures were sterile. A Wassermann reaction of the blood and cerebrospinal fluid was negative. The child left the hospital quite well on October 20.

The last recorded case is clearly one of lymphocytic meningitis (serous meningitis), but the cause is obscure. Tubercle as a cause of the meningitis can in this case be fairly excluded. The case does not correspond to the type of lymphocytic meningitis recorded by Gordon, in that the child rapidly recovered; there was no evidence that this child had recently had mumps or measles. Poliomyelitis as a cause seems probable, but it could not be proved.

The four cases just recorded serve as illustrative examples of the meningeal form of poliomyelitis. Clinically they differ from one another considerably. The first presented clinical symptoms which would suggest the acute onset of meningitis. The second presented features similar to those seen in tuberculous meningitis and died after fourteen days. The third was a fulminating case, passing rapidly into coma, and dying in three days. The fourth was a case in which the symptoms were slight, but the change in the cerebrospinal fluid was marked. The first rapidly recovered, leaving a paralysed leg. The second and third were proved by pathological examination to be cases of poliomyelitis, and the fourth case recovered completely from the lymphocytic meningitis, which was probably due to the poliomyelitic virus, but not proven to be so.

R. Morichau-Beauchant, Guyonnett and Corbin [102] give an account of two sisters, aged 4 and 5 respectively, the elder of whom had a definite attack of poliomyelitis accompanied by paralysis of right leg and left arm, and a week later the younger sister had meningitis from which she recovered completely.

(vi) *The "Neuritic" Form.*

Most observers are willing to accept the above forms of the disease, even when direct pathological evidence is not forthcoming; but few are willing to accept the "neuritic," for the clinical picture is so entirely different from that which takes place in other forms of poliomyelitis, and pathological evidence is almost non-existent.

If the presence and persistence of pain are taken as evidence of the "neuritis," then it may be asserted that there is no justification for the

title, since both these symptoms are well-recognized clinical manifestations of the common poliomyelitic lesions of the spinal cord.

If, however, there is an acute illness followed by weakness and wasting of the peripheral muscles, which affects all the extremities more or less symmetrically, and at the same time there is loss of sensation in the peripheral portion of the limbs with tenderness of the muscles, then it will be justifiable to regard the case as one of "toxic neuritis." If such a case occurred with a sudden onset or in association with a typical case of poliomyelitis in other members of the same family or household, it would be justifiable to assume that the same poison was the causative factor.

Some support in favour of the view that the virus of poliomyelitis can sometimes act as a direct toxin to the ganglion cells is to be obtained from the experimental poliomyelitis in monkeys made by Kling, Pettersson and Wernstedt, to which reference has already been made (p. 156). That the virus of poliomyelitis may sometimes act as a direct poison to lower motor neurons seems not improbable. It has been pointed out that mumps, like poliomyelitis, may give rise to a lymphocytic meningitis. Toxic polyneuritis may follow mumps, and the cases recorded by Joffroy [98], Revillion and Gallavardin [92] are instances of such.

Joffroy's case was that of a little girl, aged $6\frac{1}{2}$, who on the eighth day of mumps had pain in the limbs and violent itching. On the twentieth day a flaccid paralysis of the four limbs set in, with complete abolition of reflexes. Cutaneous sensation was blunted. The child eventually made a complete recovery.

In the cases of toxic neuritis of unknown origin in children which have come under my observation, it has not been possible to obtain experimental evidence that the child had been, or was, suffering from the poison of poliomyelitis, and in those cases which died the pathological picture is that of a primary degeneration of the lower motor neurons, not of an infiltrative poliomyelitis. Lead, arsenic, alcohol, diphtheria and sepsis are the common cause of a toxic neuritis; mumps and syphilis rarely give rise to the typical clinical picture of a toxic neuritis, and it is only these last two which can be said to act in the two different methods: (1) by producing a lymphocytic meningitis; and (2) as a direct poison to the nerve-cell.

It has not been shown either in man or in monkeys that mumps can give rise to a perivascular lymphocytosis of the spinal cord, although it gives rise to a marked perivascular lymphocytosis in the parotid gland.

It would appear that the virus of mumps, although similar to that of poliomyelitis in many ways, has no tendency to affect the nervous system, though rarely it may do so (Gordon) [95].

Wickman discusses the question of poliomyelitic neuritis at some length, and gives illustrative cases. As evidence that poliomyelitis may produce toxic polyneuritis the following cases may be quoted.

James F., aged 16, a milk-boy. In July, 1910, he had some pain in both legs. On July 30 he was taken acutely ill, vomiting for three days; had pain in the abdomen and legs. On August 3 he could not stand, and after that the legs gradually got weaker, and after a few weeks he was absolutely unable to move them, and he could not feel below the knees. He had been in bed for two and a half months, and after the seventh week in bed his legs began to get better; the arms were never much affected. He came under my care in November, 1910. He had then weakness of the arms, feeble grasp, generalized wasting; the trunk-muscles were good; the legs were wasted below the knee; he had double foot-drop, absent knee-jerks, absent ankle-jerks. Electrical changes of the character of reaction of degeneration were present in the muscles of arms and legs. The loss of sensation had cleared up when seen in November, 1910. There was no evidence of lead or arsenic. He recovered under treatment, and was discharged well in January, 1911.

The case was obviously one of toxic neuritis. The only question was, What was the nature of the toxin? The sudden onset of symptoms during the month of August suggested the virus of poliomyelitis as the cause; the proof could only be furnished by experiments on animals, and that was not done.

A. L., aged 30, was, early in May, 1913, taken suddenly ill with weakness of the legs so that she could hardly walk when she attempted to get out of bed in the morning. She had been perfectly well the night before; she had a squint at this time. Since the onset the legs had been steadily getting worse, and when seen some four weeks after the onset there were bilateral foot-drop, tenderness of the muscles, loss of all forms of sensation below the knee, and weakness and some slight anaesthesia of the hands. The knee-jerks were absent. Complete recovery took place. The clinical picture was clearly one of toxic neuritis. What the toxin was must remain doubtful, but the sudden onset suggests the possibility of the virus of poliomyelitis as the cause.

I do not think it can at the present time be asserted that toxic polyneuritis has been *proved* to be a manifestation of the virus of poliomyelitis; but considering the fact that the virus of syphilis and mumps may give rise to the clinical picture of toxic polyneuritis, and the experimental evidence that the poliomyelitic virus does in some cases act as a direct poison to the neurons—there is reasonable ground

for suggesting that polyneuritis may sometimes be a manifestation of the virus of poliomyelitis.

The question would be solved if there was a simple specific blood reaction for poliomyelitis, and it were possible to carry out the test over a sufficient number of cases; but such has yet to be determined.

(vii) *Abortive Form.*

In this country and in London, where it may be said that poliomyelitis has never become epidemic, it is not possible to describe an abortive type of the disease. Reece, in the Stoke Rivers epidemic in Devon, described a large number of cases of indefinite illness which might possibly be cases of this nature; but the proportion of these to actual cases of paralysis was so large that it is difficult to accept them as such.

Wickman, in the Swedish epidemic of 1905, and Kling, Pettersson and Wernstedt in that of 1911, were able to recognize a considerable proportion of abortive cases as occurring in the members of households in which definite cases of poliomyelitis were present.

The picture of the abortive type as given by Wickman corresponds in general with that of the initial stages of typical poliomyelitis. The attack as a rule is acute, and accompanied by fever, headache and malaise. In some cases these symptoms are associated with others, such as rigidity in the neck, pain in the neck, back, loins and limbs, and paræsthesia, which point to infection of the nervous system.

These symptoms are not followed by paralysis. The patient usually recovers within a few days, and no trace of the disease remains, except prostration, which may be prolonged. The abortive case thus presents only symptoms of general infection, and no real localizing signs. In the abortive cases not infrequently symptoms attributable to meningeal irritation arise. More or less opisthotonus may occur. Tenderness of the extremities is common. Nausea, vomiting and diarrhoea and other gastro-intestinal symptoms have frequently been observed in association with the abortive types.

Wickman distinguishes the following varieties of the abortive type:—

- (1) Cases running the course of a general infection.
- (2) Cases in which signs of meningeal irritation are especially prominent.
- (3) Cases accompanied by distinct tenderness.
- (4) Cases with gastro-intestinal disturbances.

(2) *Relapsing Cases of Poliomyelitis.*

Reference has been made to the so-called "jump" cases of poliomyelitis in which the disease is not steadily progressive, but remains stationary for a day or two, and then rapidly advances.

Relapsing cases differ somewhat from the above in that the patient improves in the interval, and it is thought that he is going to recover. Then fresh symptoms develop, which may again clear up, and then a further relapse may occur. A very good instance of such a relapsing case with a pathological verification is recorded by Reginald Miller [100] :—

A little boy, aged $3\frac{1}{2}$, was taken ill on September 14, became drowsy, unable to move. The lower limbs were completely paralysed and the neck muscles partially so; the arms and respiratory muscles were unaffected. The boy progressed favourably till September 25th, when he became dyspnoëic and cyanosed, and it was found that the intercostals and rectus abdominis were paralysed. He improved, but on October 1 a second relapse occurred, and the muscles of the left shoulder became powerless. From this date there were no fresh signs until October 17, when there developed suddenly a very marked nystagmus, lasting three to four days, gradually becoming less and less marked until the twelfth day, when it was no longer observable. During his further stay in hospital he steadily improved, and was discharged on January 3. A week later he developed broncho-pneumonia and died on January 12. The pathological examination was made by Dr. Gordon Holmes, and the specimens showed the typical appearance of a poliomyelitis, not only in the cord, but also in the medulla, pons, cerebellum, and mid-brain.

(3) *The Occurrence of Second Attacks of Poliomyelitis.*

It is well recognized that progressive muscular atrophy may occur in a patient who during early life has been the subject of poliomyelitis. A series of twenty-eight such cases is recorded by Potts [108] and they are not very rare. In eighteen the atrophy occurred in the limb previously affected; in the remainder in some other part.

The occurrence of a second attack of poliomyelitis is very rare; no such case has come under my observation. Eshner [88] records the case of a girl who had an attack of poliomyelitis when 25 months old, the right lower extremity being affected, and a second attack, attributed to a fall, in the hands eleven years later. Oulmont and Bandouin [105] record another case in a man, aged 60, who within a year had a second attack and died. The *post-mortem* showed changes in the anterior horn and in the muscles. A third case is recorded by Sanz [111], in a girl who had the first attack when 1 year old, affecting left leg and foot,

and the second attack at the age of 15, when the right arm and right leg were affected. Not one of these cases appears to me to be very convincing or to bear critical investigation.

(4) *Intra-uterine Poliomyelitis.*

The occurrence of poliomyelitis in the foetus during intra-uterine life is very difficult to prove. Not a few cases come under observation in which the paralysis is stated to have been observed immediately after birth; and when the child has come under observation the clinical features closely resemble the late effects of a poliomyelitis.

Flaccid paralysis of one arm due to birth injury is far from uncommon in infants, and in most cases is probably due to injury of the roots of the brachial plexus. It has been shown by Herbert Spencer, however, that hæmorrhage into the grey matter of the spinal cord in children dying at birth or soon after delivery is not uncommon, and it is reasonable to suppose that in some of such cases which survive the paralysis may be due to hæmorrhage into the grey matter of the cord, and Boyer [84] has proved that such was the case in one instance.

The clinical evidence which is here brought forward in support of intra-uterine poliomyelitis is admittedly open to question, in that it is based on the statement of the mother of the child and not on personal observation, but the pathological evidence is complete.

The question of poliomyelitis occurring during intra-uterine life was discussed in a paper published in *BRAIN*, 1910 [81], and the case in which the diagnosis was made is there fully reported with a pathological examination proving that the condition was one of poliomyelitis.

Another case of poliomyelitis of the right arm and left leg occurring during intra-uterine life has since come under my observation, but no further pathological proof has been obtained:—

A. S., the second of three children, was born in September, 1911. The mother was not attended by a doctor. The mother states that she did not notice the weakness of the right arm until the child was 2 months old, but this child, unlike her other children, never made any attempt to move its arm. Wasting of the left leg was noticed some months later, but no attention was paid to this until the child was 18 months old, when it was found that it could not walk. The child had no acute illness from the time of birth till 2 months old, when the paralysis was first remarked. The birth was easy, and there is no evidence of injury during parturition. The child is intelligent and well nourished, has a complete flaccid palsy of the right arm, with considerable wasting, and a flaccid palsy of the left leg, also accompanied by wasting. The knee-jerk on the right side is active, on the left side absent. The child presents

the typical features of a case of poliomyelitis. The question which arises is whether this condition occurred during intra-uterine life, at birth, or subsequently. It seems impossible, considering the severity and wide extent of the lesion, that the child could have had an acute attack of poliomyelitis which should have escaped the mother's attention between birth and the second month of life. The paralysis of the right arm and the left leg is not such as one would expect from a birth injury. The case is clinically very similar to that already recorded, in which the *post-mortem* showed changes in the spinal cord characteristic of old poliomyelitis.

A third case with complete flaccid palsy of the neck muscles came under my observation in which the weakness had been present from the time of birth, the child dying when aged 2 years. No pathological examination was permitted. Further evidence on this subject is required.

(5) *Herpes Zoster in relation to Poliomyelitis.*

It is well recognized that herpes occurs not only in association with a localized paralysis in the same individual, but is also liable to be present in an epidemic form at the same time of year and in the same locality as poliomyelitis.

Garrow [124] described such a prevalence in the epidemic on the west coast of Cumberland in 1910. Brincker [120], in his report on the Stepney prevalence in 1914, states that herpes zoster was also prevalent at the same time. Many examples of herpes zoster of the forehead and face in association with ocular paralysis are on record, others of cervical herpes with facial paralysis, others of trunk or limb herpes with trunk or limb paralysis.

It is quite certain that many of these cannot be attributed to the virus of poliomyelitis; some may be vascular, as Farquhar Buzzard [123] suggests, others are probably syphilitic, as in the case recorded by Parkes Weber [117], but there are others with an acute and sudden onset which might be attributed to poliomyelitis; and Ramsey Hunt [127] has described acute posterior poliomyelitis of the geniculate and neighbouring ganglia.

Stanley Barnes [119] has described in considerable detail a case of right facial paralysis with herpes in the distribution of the third and fourth cervical on the same side in a man, aged 40, who recovered completely.

Alex Bruce [122] described a case of herpes of the seventh and eighth intercostal spaces, associated with weakness of the limb on the same side, with a dissociated form of anæsthesia; he hypothesized a lesion at the base of the posterior horn which may give rise to such a group

of symptoms, involving the fibres of the pyramid as they pass from that structure to the anterior horn cells.

Frederick Taylor [128] recorded in 1895 a case of shingles followed by paralysis of the abdominal muscles in a man, aged 60. The paralysis of the muscles was first noticed about three weeks after the appearance of the rash. Three years later the paralysis was still present. He mentions similar cases recorded by Broadbent and Joffroy.

Further, Head and Campbell [126] have shown pathologically that the changes in the posterior root ganglia producing herpes are similar to those found in poliomyelitis.

Griffon [125] examined the cerebrospinal fluid in eleven cases of herpes zoster and found more or less marked lymphocytosis in all. It is a striking fact that nearly all the recorded cases of paralysis associated with herpes are in adults, and in many cases in elderly people.

In childhood the simultaneous occurrence of herpes zoster with poliomyelitis is rare, and the following is one of the few cases I have seen in childhood:—

A. R., aged 7, was taken ill with "influenza" in December, 1914. He had great pain in the right shoulder and a rash over the right side of the chest. When first seen, six weeks after the onset, there were marked weakness of the shoulder muscles and the remains of the rash over the thorax, indicated by pigmentation and slight thickening of the skin. The rash cleared up entirely, but a permanent weakness of the right shoulder remained.

A rash sometimes accompanies poliomyelitis, formed of small vesicles, widely distributed over the trunk and limbs, mostly on the former. Brown [121], in Toronto, described a small, shotty papule with a tiny inflammatory base which might or might not go on to vesiculation in association with poliomyelitis. If it did, the vesicle resembled a small chicken-pock, containing clear fluid.

Association of Herpes Zoster with a Generalized Eruption of Varicella-like Spots.—Many cases of herpes zoster associated with, or followed by, a generalized vesicular eruption have been described. These have recently been collected by Parkes Weber [118], who records a case of oculo-motor paresis and herpes associated with a generalized eruption.

It has been suggested that herpes zoster is a modified and localized form of varicella, and Johann von Bokay published nine observations in support of this view, and other writers quote similar cases. Weber discusses but does not favour this view. Whatever the pathology may be, the important clinical observations remain; that cases of herpes

zoster and a diffuse eruption like varicella occur associated with a localized paralysis of muscles in the same individual.

That some of these cases may be due to the virus of poliomyelitis is possible, but from the fact that the herpes commonly precedes the paralysis, and that the larger proportion of the cases is seen in persons of advanced years, it seems that toxic agents other than poliomyelitis must play an important part in the production of the associated symptoms. It is in cases of this nature that some simple serum test would be of such diagnostic value.

(6) *Cerebrospinal Fluid in Poliomyelitis.*

The examination of the cerebrospinal fluid in cases of poliomyelitis has yielded variable results. In some cases the fluid has been normal, in others there has been an excess of albumin, with a moderate increase of lymphocytes, in others again a very large increase of these cells.

The condition of the cerebrospinal fluid has varied not only with the time after the onset of symptoms at which the fluid was examined, but also with the nature of the case, the cases with the most marked meningeal symptoms tending to yield the largest cell count. Netter states that in the early stages of poliomyelitis the cerebrospinal fluid is definitely fibrinous and rich in cells, many of which may be polymorphonuclear.

Gay and Lucas [94] have studied the cerebrospinal fluid in monkeys during the incubation, the prodromal, and the acute stages of the disease, and in *eleven human* cases in the pre-paralytic stages. In these eleven cases the cell count varied from 55 to 580 per cubic millimetre, and the percentage of mononuclears from 75 to 100.

Peabody, Draper, and Dochez [107] examined 233 fluids from sixty-nine cases. The number of cases seen in the first week (dating from onset of symptoms and not of paralysis) was forty-three; in the second week, forty-five; in the third week, forty; in the fourth week, thirty. Four cases were seen in the pre-paralytic stage, and two in abortive cases.

The examination of the cerebrospinal fluid included pressure, number of cells per cubic millimetre, types of cell, chloride, reduction of Fehling, and globulin contents. Almost all the fluids were clear, only a few showed any opalescence. A web-like clot was seen in a small proportion of cases and in the early stages of the disease. It bore no relation to the globulin content. The pressure was usually somewhat above the normal, but the observations were unsatisfactory owing to variation due to respiratory efforts or crying. Chlorides were present in normal amount. Every fluid showed the normal reduction of Fehling solution.

The type of cell is almost always mononuclear early in the disease, but in the pre-paralytic period the polymorphonuclears may amount to 80 to 90 per cent. of the total.

The commonest type of fluid seen in the whole series is one with a normal or slightly increased cell count and a well-marked globulin reaction. Two other types are seen: (1) with a high cell count and a normal or very slight globulin reaction; (2) a fluid with a normal or low cell count and a very marked globulin reaction. Twenty-six cases showed a slight globulin reaction and a cell count of 50 or over.

The following conclusions are deduced: fluids taken during the early days of the disease, and especially before the onset of paralysis, tend to show an increased cell count with a low or normal globulin content; in the early stage the polymorphonuclear cells may amount to 90 per cent. of the total; most fluids, however, show almost exclusively lymphocytic and large mononuclear cells. After the first two weeks the cell count drops to normal, and there is frequently an increase in the globulin content. A slight increase in the globulin may persist for seven weeks or longer. Analogous changes may be found in the fluid of abortive cases. All fluids examined reduced Fehling's solution.

Experience drawn from a series of cases in which the cytological examination was made by Dr. Forbes and Dr. Nabarro, at the Children's Hospital, mostly two to three weeks after the onset, would indicate that at that period the cerebrospinal fluid had in most cases returned to the normal. Even in the acute cases the increase in the number of lymphocytes has been small, as has also been the amount of albumin.

Forbes [91], in a series of thirty-three specimens from thirty cases of poliomyelitis, examined at periods of from three days to six weeks after the onset, found in twenty-four specimens the fluid was clear and free from clot. In eight trace of blood was present. In one specimen a very fine web formed on standing.

Cytological examination showed the presence of lymphocytes slightly in excess of the normal (1 to 5 per cubic millimetre), but in six specimens there was a definite increase above the normal, and in another six no cells, or only the normal few cells were present.

Netter points out that it is in the meningeal type of the disease that the cerebrospinal fluid shows most changes, and he noted that in some epidemics the meningeal type may form a considerable proportion of the cases; he quotes instances of 50 per cent. and over.

The meningeal type must, I think, be rare in England. Of cases

seen during the year 1915 at the Children's Hospital, only two presented symptoms suggestive of meningitis. One died and the other recovered.

The diagnostic value of the examination of the cerebrospinal fluid in cases presenting symptoms of cerebrospinal disease is considerable.

In the first place it separates the cases with meningeal symptoms into two large groups: (1) Those in which the cerebrospinal fluid is turbid and contains a high percentage of polymorphonuclear cells; and (2) those in which the fluid is clear or slightly cloudy, and contains an increased percentage of cells, lymphocytic in character.

The first group is due to the presence of one of the infective organisms, meningococci, pneumococci, streptococci, influenza, *typhosus* or *coli* bacilli; the second to tubercle, syphilis, poliomyelitis, mumps, sinus—thrombosis, measles, tumour, and late cases of infective meningitis.

It has been shown that rarely a case of meningococcal meningitis may, in its early stages, give a fluid which is clear and contains but few cells; such cases are rare, and in a long series of meningococcal infection I have never come across one, although I have observed such a case in the earliest stage of a pneumococcal meningitis. As has already been stated, the reverse is also true—viz., that a case of poliomyelitis may, in its earlier stages, show a high polymorphonuclear count.

The important class to consider is the second—i.e., those in which there is an increase of the lymphocytic cells.

There can be little doubt that the condition which most frequently gives rise to a lymphocytic increase in the cerebrospinal fluid is a *tuberculous meningitis*—if tubercle bacilli are found, diagnosis is certain; but with a negative return the diagnosis is still uncertain. In tuberculous meningitis the reduction of Fehling solution is usually absent or delayed, in poliomyelitis the reaction is almost always present and immediate. The percentage of globulin is variable, but is usually higher in tuberculous meningitis.

In syphilis there is a marked lymphocytosis; but the chronicity of the case, with the high globulin content, together with the positive Wassermann, render the diagnosis clear.

The experimental work of Gordon [95] and the clinical observations of Anthony Feiling [89] on cases of mumps and on a fatal illness in children associated with acute interstitial parotitis are important in this connexion, for in both a lymphocytic meningitis may be present. Gordon took washings from the mouth and saliva from ten cases

of mumps from the first to the sixth day after onset of the disease. Having passed these through a Berkefeld filter, he injected the filtrate intra-cerebrally into ten monkeys. Four of the monkeys developed meningitic symptoms, and in one the cerebrospinal fluid was found to contain 1,500 white cells per cubic millimetre, 82 per cent. with lymphocytosis, 12 per cent. polymorphonuclears. The changes found in the nervous system were infiltration of the pia-arachnoid with lymphocytes; the perivascular infiltration characteristic of poliomyelitis was absent. There was no infiltration of the grey matter.

Gordon concludes that the experiments seem to justify the view that in a proportion of cases of mumps a virus occurs in the saliva that passes through a Berkefeld filter, and is capable of producing in the monkey, by intra-cerebral injection, a lymphocytic meningitis, together with hyperæmia of the central nervous system and acute degenerative changes in a proportion of the neurons. Furthermore, if the animal lives long enough acute interstitial parotitis may be produced. Mumps is therefore probably due to an ultra-microscopic organism.

Gordon next deals with a series of twelve cases of acute and fatal illness with cerebral symptoms in children, the cerebrospinal fluid showing a marked lymphocytosis, death taking place in twenty-four hours to twelve days.

The cerebrospinal fluid in six cases was clear and showed no bacilli; in three cases there was no increase in the number of cells, whilst in two it was 446 per cubic millimetre and 6,000 per cubic millimetre respectively. After death none of the ordinary causes of meningitis was found; the central nervous system appeared congested. In all the eleven cases in which the cerebrospinal fluid was examined *post mortem*, the cells present were found to be lymphocytic. Section of the brain and spinal cord showed no infiltration of the substance, the only change being a variable amount of chromatolysis in the cells. In one case only was a perivascular infiltration found at one point in the medulla.

In eleven of the cases foci of acute interstitial inflammation were found to be present in one or more of the salivary glands.

From five of the eleven cases monkeys were inoculated intra-cerebrally with an emulsion of pieces of the parotid gland and spinal cord passed through a Berkefeld filter. The result of these experiments was negative. The nature of the virus to which the death of these children might be attributed must remain doubtful.

Feiling [89] describes a case of lymphocytic meningitis following mumps in which the cells numbered 2,500 per cubic millimetre,

lymphocytes amounting to 96 per cent. Ten days later the number of cells had fallen to 20 per cubic millimetre, and the child recovered.

Measles again may be followed by acute cerebral symptoms, and the cerebrospinal fluid may show a high lymphocytic count.

Sinus thrombosis, cerebral abscess, infective conditions in the region of the brain (mastoid disease), and cerebral tumours, when they come in close relation to the ventricles, give rise to a lymphocytic cerebrospinal fluid.

The knowledge that a serous meningitis is present may not be of great diagnostic value, but a serous meningitis of acute onset which rapidly clears up is strongly in favour of poliomyelitis.

(1) *Blood in Poliomyelitis.*

Peabody, Draper, and Dochez [107], who examined the blood of patients with poliomyelitis, found a constant and marked leucocytosis. In several instances the count has been as high as 30,000. In only one case was there a definite leucopenia. Besides the increase in the total number of cells there has been an equally constant increase of polymorphonuclears of 10 to 20 per cent.

The visceral lesion of poliomyelitis showing the active part of phagocytosis played by the polymorphonuclear cells is perhaps sufficient cause for the polymorphonuclear increase in the circulating blood.

In view of the fact, however, that the brunt of the body's attempt at defence falls upon the lymphatic system, and that the cells which are assembled at the point of attack seem to be lymphocytes, one might be led at first to expect a lymphocytosis in the blood. On the other hand, the great destruction of lymphocytes which is evident in the visceral lesions suggests that these cells are relatively few in the circulation because they are constantly being withdrawn to meet the invasion of the virus at its various points of attack. It will require a more fundamental knowledge of the kind of reaction the body develops to this type of infecting agent before a correct explanation of the blood picture can be made. At all events, while the blood picture in poliomyelitis is perhaps not any more specific than is the spinal fluid, it is helpful. If taken in connexion with other available evidence, a leucocytosis of 15,000 to 30,000 is distinctly suggestive of the disease in question, especially if the polymorphonuclear cells are increased at the expense of the lymphocytes.

Other observers have found no change or a leucopenia, and it seems probable that in most cases the changes in the blood are inconsiderable.

Few observers have had the opportunity of examining the blood in the pre-paralytic stage of the disease such as fell to the lot of Peabody, Draper and Dochez.

CHAPTER VII.—TREATMENT.

(1) *General.*

Recognizing that poliomyelitis is an acute specific fever, having an incubation period of four to twelve days, the patient should be isolated. In hospital it is not necessary to place the patient in a separate ward, and bed isolation is sufficient to prevent the chance of infection. Personally I have never seen poliomyelitis either spread or arise in the ward, although I know of one infant who had been months in an institution develop the disease, there being no other cases in the ward, although there were chronic cases in the hospital. Peabody, Draper and Dochez isolated their patients in separate wards and dealt with them in the same way as other acute infectious diseases.

As the virus is known to exist in the nasal and buccal mucous membrane, it is well to pay careful attention to these and to any discharge therefrom, and to clean the nose and mouth two or three times a day with a 0·2 per cent. solution of permanganate of potash or chlorine water.

The acute stage is often attended by fever, sometimes by convulsions and pain, with rigidity of the neck and spine. Pain may be intense, sometimes so severe that the patient dreads the least touch of the bed or bed-clothes, or movement of the affected limbs. At times the patient may be unconscious, following a convulsion, with marked head retraction, opisthotonos, and signs of meningitis. As has been pointed out, the diagnosis in such cases depends upon the examination of the cerebrospinal fluid. Sometimes, owing to the rigidity of the back, it may be difficult, if not impossible, to do a lumbar puncture, and in order to perform this it is necessary to administer an anæsthetic. Lumbar puncture by itself often seems to relieve the most acute symptoms. It therefore is useful not only as a method of diagnosis, but also as a means of treatment.

(2) *Serum Treatment.*

It has been shown experimentally that immune serum has no power to prevent the development of the disease when injected simultaneously, or after the virus has been injected; Flexner and Amoss [132] have

shown that the intrathecal injections of an immune serum are effective when introduced in the pre-paralytic stage in delaying and preventing poliomyelitic infection in the monkey. This method of intraspinal injection of immune serum has been used with success by Netter [136] in cases of poliomyelitis of the acute ascending variety. In one case eight injections were given of from 4 c.c. to 12 c.c., obtained from a series of old cases of poliomyelitis.

The method is as follows: some 20 c.c. to 30 c.c. or more of blood are obtained by venupuncture from a patient who has passed through an attack of poliomyelitis (the length of time after the attack is not important, for it has been shown that the blood preserves its antitoxic properties for several years). The serum is separated by allowing the blood to clot and by centrifugalization. The serum is warmed to 98° F. Lumbar puncture is performed on the patient and an amount of cerebrospinal fluid removed corresponding to that of the serum which it is proposed to inject—usually about 10 c.c. The serum is now slowly injected and the bed of the patient tilted so as to allow it to gravitate cerebral-wards. The injection can be repeated daily from three to four days or more.

There is little or no difficulty in carrying out the treatment. The difficulty is to obtain an old case of poliomyelitis who has already been tested and given a negative Wassermann reaction, and who is willing to give the necessary blood at the same time as a suitable case of acute poliomyelitis presents itself for treatment.

It is useless to carry out this treatment when the disease has already become quiescent, and the typical cases for such are either—(1) presenting symptoms of an ascending or progressive poliomyelitis, or (2) presenting meningeal symptoms, or (3) (if the diagnosis can be made) in the pre-paralytic stage.

I have on two occasions carried out the treatment: once in a baby with a lymphocytic meningitis; the child recovered, but with considerable mental defect. The second was a case of widespread and extending poliomyelitis under the care of my colleague, Dr. Still. This child, I am informed by Dr. Sidney Smith, made an almost complete recovery, but that cannot necessarily be attributed to the serum.

This method of treatment can be effective in a very limited group of cases only during the acutest stage, and special circumstances are needed for carrying it out—i.e., a suitable giver and laboratory facilities.

The possibility of employing the sera of animals has been considered. Flexner and Lewis found that the sera of horses and rabbits had no

viricidal action. Sheep's serum was slightly active and might be increased by injections of the virus, but the degree of activity appears to have been small.

(3) *Drugs.*

The acute pain associated with the disease can to a large extent be relieved by careful support of the limbs and of the patient, and of the arrangement of the bed. Aceto-salicylic acid is the drug which in my experience gives most relief; other coal-tar derivatives are of value, but in some cases morphia is needed. The administration of hexamine has been advocated on experimental grounds, for it has been shown that it passes into the cerebrospinal fluid, and that in animals it tends to delay, if it does not prevent, infection of the spinal cord by pathogenic organisms. It should be administered in large doses, 10 gr. every four hours to young children. There is no doubt that hexamine reaches the spinal fluid, but there is some doubt that it is present in that fluid in the active form of formaldehyde or that it has any beneficial effect. The only disadvantage in the administration of this drug is that it occasionally gives rise to hæmaturia.

(4) *Rest, Posture, Re-education.*

There can be no doubt that rest is the most important method of treatment. The too early movement may in some cases restart the disease which has become quiescent, and relapses have been produced in this way. A child with an acute attack of poliomyelitis should be kept absolutely at rest in bed for at least three weeks; the length of time necessarily depends on the severity, but even in the slightest cases movement before this time is inadvisable. Though bed may give rest to the body generally, it does not necessarily afford the complete physiological rest required for recovery of a muscle, and hence it is essential to consider the principles on which such rest can be secured. Sherrington [138] has shown that the normal skeletal muscle is possessed of a degree of tension or tone, and that there is a reciprocal innervation of muscles, so that when the flexor contracts there is an active relaxation or inhibition of tone in the extensors. The tone of the muscles is largely dependent on afferent impulses. If the extensors are paralysed and the limb lies in the flexed position, there is a tendency for the extensor to become stretched, whilst the flexor becomes more contracted; but not only is there an actual stretching of the paralysed muscle, but there is in all probability an active inhibition giving rise to a further loss of tone. The anatomist, William Mackenzie, expresses

the same in somewhat different language. The muscle adjustments are so fine that immediately the nerve-cell governing the action of the flexor is affected, the extensor opponent begins to over-act, and this over-action must be prevented for the following reasons: (1) It does not allow complete rest of the affected anterior horn-cell; (2) by over-stretching the affected muscle it interferes with its recovery. Robert Jones [134] expresses the same facts by a mechanical metaphor, saying: "The whole reflex apparatus by which the spinal nerve-cell and muscle react on each other to their mutual benefit is put out of gear." And he insists on relaxation of the paralysed muscle; but as William Mackenzie [135] points out, relaxation is only the beginning of treatment, and more than this is required, and that is re-education of the paralysed muscle. All are agreed that a stretched muscle is at a disadvantage and will not recover its power until relaxed.

Posture.—Posture is therefore the great factor in securing physiological rest to a muscle, and it is important to consider what is the *zero position* of any given muscle. Mackenzie defines the zero position as the position of anatomical rest in which the individual muscle itself is relaxed, and both its own action and that of its opponent's prevented. Sherrington has shown that the distribution of tonus is arranged on a plan of strict co-ordination, and that reflex tonus embraces those movements which counteract the effect of gravity, and that postural contraction can be maintained for long periods without fatigue. A position which can be maintained without fatigue must be the position of rest.

Application of the Principles of Rest, Posture, and Re-education in the Treatment of Paralysed Muscles.

Rest, posture and re-education are the important methods of treatment. Various methods have been adopted for keeping the paralysed muscles at rest and in a state of "relaxation." Simple rest in bed is regarded by some as sufficient. Others place the limbs between sand-bags, so as to prevent movement and misplacement of the limb. Others place a board at the bottom of the bed, which is often effective in keeping the foot in the dorsi-flexed position. Various splints of metal and other material have been used. Some medical men have advocated placing the patient or the limb into a plaster of Paris mould, so that no movement is possible. Robert Jones insists that the paralysed muscles must be placed into the position of complete relaxation, and that any deviation from this position, even momentary, is harmful. Success

has, and will, attend all these methods, but they all have the same disadvantage that they tend to immobilize the patient for the period of many months, and give the child but little chance of physiological action and re-education of the muscles, which may have been greatly or slightly affected.

Plaster-of-Paris.—The use of plaster-of-Paris as a means of support is easy, and in selected cases of poliomyelitis is most valuable. In some the limb can be placed into plaster-of-Paris in the ordinary way; in others, a removable plaster-of-Paris splint can be made so that the limb is kept in the zero position until recovery has taken place, or until a more permanent splint is made, and treatment by massage, passive and resistance movements can be carried out in the meanwhile.

Splints.—The practical application of the above principles has been carried out by the following method: The paralysed limb or limbs are placed in a light celluloid splint accurately fitted to the limbs as soon as it is possible to make the cast after the onset of the disease. These splints were first made by M. Calot [131] in France, and introduced into this country by Gauvain [133], who employed them extensively in the treatment of tuberculous joints, and most kindly instructed me in their use [130].

It is not my intention to enter into any detail here as to their construction, but seeing that the splint is to serve in most cases not only for keeping the muscles at rest, but also as a support in walking, it is essential that the position of the limb should be such that progression is possible. The splint is moulded on a plaster-of-Paris cast of the limb, and it is the making of this cast which is important, for the limb must be in the *zero position*, or in other words, the position normally assumed to counteract the effect of gravity when the patient is in the erect position. That position, so far as the legs are concerned, is one of *slight flexion of the knee with the foot at right angles*, or at an angle slightly greater than a right angle to the tibia (fig. 36).

The advantages of this form of splint are: (1) That they maintain the muscles constantly in a position of rest, for they can be worn day and night; (2) they do not immobilize the patient, so that walking exercise can be carried out without the liability to produce deformity or stretching of the muscle; (3) they are easily removed and replaced, so that other methods of treatment can be carried out; (4) no special boots or shoes are required (fig. 37).

The aim of treatment has been to keep the limbs in a normal position and free from deformity whilst recovery is taking place, and



FIG. 36.—Photo of child with flaccid paralysis of both legs in celluloid splints. Note that the splint is taken sufficiently high so that the weight of the body is supported on the tuber ischii, the knee is slightly flexed and the foot is at right angles to the tibia.



FIG. 37.—Photo of same child in walking machine. The early stage of the re-education of the child in walking.

the result has to a great extent been attained. In the legs with paralysis of the muscles of the thigh and below the knees no great difficulty arises. All the mal-position of the foot and knee can be prevented. It is somewhat difficult to prevent the outward rotation and abduction of the leg below the knee in those cases in which the biceps femoris is relatively good compared to its antagonists. So long as the child has remained in the hospital no deformity has arisen, but under home conditions in which the splint is left off and massage and



FIG. 38.—Photo of same child at a later stage, when the child can walk easily and rapidly with the machine.

educative movements not maintained, the deformity readily occurs and is not easily corrected. The flexor and extensor muscles of the hip are, however, the most difficult to keep in a position of relaxation. So long as the child is lying in bed the tendency for the flexors of the hip to contract can be prevented, but if the child is allowed to sit up the flexors tend to assume a contracted position, with the result that the hip is flexed on the pelvis (fig. 29, p. 170). In such cases it is best to allow the child only to assume the erect or lying position. The erect position can usually be assumed by means of a walking machine (fig. 38), whereby

the child supports the weight of the trunk on the hands and allows the limbs to swing. Such a position tends to re-educate and bring into function not only the flexor and extensor movements of the thigh, but also all the muscles of back and abdomen. Careful attention to the extensors of the legs, with regular massage and movements, will to some extent prevent this contraction, but in severe cases, in which the extensors are completely paralysed and the flexors but little affected, the flexors come into action, and when the child attempts to assume the erect position lordosis is produced. I am rather of opinion that in these cases it is best to put the flexors out of action by division, and if this be done early it gives the opposing extensor a greater chance of recovery and prevents any displacement of the hip-joint, which is likely to occur if the contracture is of long duration.

A still more difficult condition to deal with is that of paralysis of the flexor of the hip with good power remaining in the extensor. This is fortunately a very rare manifestation. It is possible to place the child in a fixed position with the knees and thighs flexed, and this has been done and maintained for some months; but a few days after the child is taken out of plaster the position of hyper-extension is again assumed. Allusion to this form of deformity has already been made in the clinical section of these lectures, and in the case referred to treatment was completely unsuccessful (fig. 30, p. 170).

Abdominal and back muscles.—If these muscles are seriously involved, standing and walking are almost impossible. On the other hand, there is no exercise which is so effectual in re-educating them as that of attempting to balance and assume the erect position. Deformity can be prevented by the recumbent position and by extension, but should the affection of the muscles be severe the child will need artificial support to prevent deformity when it assumes the erect position.

Walking exercise and the erect position.—When once the legs are splinted it is possible to get the patient into the erect position, and such allows of the physiological use of the back, trunk and pelvic muscles. Such walking exercises are carried out by the use of a walking machine, which supports the child both physically and morally, for it is important to give the child complete confidence in itself (figs. 37, 38, 39).

Arms.—The most common form of paralysis of the arm is a paralysis of the deltoid, biceps and shoulder muscles, while the forearm remains relatively good. In order to relax the deltoid the arm must be abducted from the thorax, and it is usual to place the hand behind the head so as to secure this. I have adopted two methods in dealing with these cases:

(1) To make a celluloid splint which will hold the arm abducted and flexed (figs. 40 and 41); (2) a Fairbank splint, which keeps the arm in this position (fig. 42). The disadvantage of the former is that it is difficult to make, and the angle of the abduction cannot be altered. The advantages of the latter are that it is easy and cheap to make, and is readily adjusted to any angle required. The arm should be kept in that



FIG. 39.—Photo of child with poliomyelitis learning to walk. Considerable lordosis has been produced owing to the long standing contraction of the flexor of the hips.

position day and night for at least twelve months. If at the end of that period no improvement has taken place it is improbable that any recovery will occur, and the arms can be placed in the flexed position at the side, so that the hand may be of greater service.

Neck.—The isolated paralysis of muscles of the neck is a somewhat rare manifestation. A child with this affection is quite unable to walk, owing to the inability to maintain the balance. A collar which will hold the head in the erect position not only places the paralysed muscles at rest in the zero position, but also prevents the head being jerked



FIG. 40.—Child with paralysis of the deltoid and biceps muscles in celluloid splint.™ The splints tend to keep these muscles relaxed and prevents the over-action and contraction of the latissimus dorsi and pectoral muscles.



FIG. 41.—Man with poliomyelitis of the shoulder muscles of the left arm. The splint has an additional support from a strap and band round the right shoulder.

either forward or backwards, thus throwing the child to the ground (fig. 43).

The above are simply instances of the application of the principles that the paralysed muscle must be placed in the position of rest. Almost every case varies in the muscles paralysed, and needs individual thought as to the position in which the limb should be placed. If, however, medical men will adopt the practice of placing the limb in a splint in a position of rest *at an early stage of the disease*, not only will the recovery of the muscles be more complete, but the greater portion of the deformities which one now sees as a result of poliomyelitis will be prevented.

Re-education of movements and muscles.—The re-education of the paralysed muscle is of great importance. With a severely paralysed muscle it is essential in early stages to place the limb in such a position that the load on the muscle is at its minimum; for the sake of example, with a paralysed biceps of the arm the upper arm must be in the horizontal position, as it is when the patient is recumbent, the forearm in the vertical position at right angles. Only a very small force is now required to overcome gravity and flex the arm. The angle is slowly increased and graduated to the power of the muscle as it slowly recovers. A bath is an excellent place to practise the re-education of muscles, for the weight of the limb is supported and ranges of movement are possible which are impossible without the support of the water. Education will gradually increase these movements.

(5) *Massage.*

In massage—and under this heading I include all active and passive and re-education movements—we have most valuable methods of maintaining the nutrition of the muscles and assisting recovery whilst regeneration of the damaged neurons is taking place. Friction and warmth to the skin stimulate, and are of great service in maintaining the circulation.

Warm baths and douches.—Warm baths and douches have the same effect, and are of service in relieving pain and allowing of movement in an otherwise painful joint.

(6) *Electricity.*

All forms of electricity have been employed in dealing with cases of poliomyelitis: some may be of service, others are useless, others again are harmful. It is probable that the galvanic current is of service



FIG. 42.—Child with poliomyelitis of the right deltoid and bicep in Fairbank splint. The advantage of this splint over the celluloid is that the angles can be easily adjusted.



FIG. 43.—Boy with flaccid paralysis of neck muscles in celluloid collar.

in stimulating paralysed muscles to contract, but the current, when sufficiently strong to cause a paralysed muscle to contract, gives considerable pain to children and is ill borne, and the advantages gained by no means compensate for the emotional disturbance produced.

Faradism and the alternating currents may be said in most cases to be directly harmful. They cause the active contraction of unparalysed muscles, whilst the paralysed muscles do not react; thus the paralysed muscles are stretched.

The skin stimulation to which other forms of electricity give rise may be of some benefit.

(7) *Other Methods of Treatment.*

It is not my purpose to deal with the later stages of paralysis which require some mechanical replacement of and support for the paralysed muscle, nor with the surgical aspect of the treatment of the late effects of poliomyelitis by tendon lengthening, tendon transplantation, tendon fixation, artificial ligaments, nerve-grafting, arthrodesis, and the like; but I am convinced that if the line of treatment above advocated is extensively adopted, recovery of power in the muscle will be greater and a large proportion of the deformities which are now seen in cases of poliomyelitis will be prevented.

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EDITOR.

BRAIN.

PARTS III and IV, VOL. 39.

THE POSSIBLE FUNCTIONS OF THE CEREBROSPINAL FLUID.¹

BY PROFESSOR W. D. HALLIBURTON, M.D., F.R.S.

So much has within recent years been written about the cerebrospinal fluid that I must apologize for my want of originality in selecting that subject for this address. But however hackneyed the subject, we are still far from possessing complete knowledge as to the functions and significance of the fluid. From the pathological as well as from the physiological point of view, we at least know that this remarkable fluid is one of the greatest importance, and its careful examination in many diseases has yielded results of inestimable value. During the last few years it is a subject at which I have myself worked, and I have been fortunate in securing as my collaborator such a skilful and accurate experimenter as my colleague Professor W. E. Dixon.

One cannot work at any subject for any length of time without speculating beyond actually observed data. It is the safest rule to keep ideas of this nature to oneself, but there are some occasions when it is permissible to speak rather more freely; this is one of them. I happen to be the unworthy occupant of a presidential chair, and for an hour or less I shall be free from contradiction and criticism, so I propose to inflict upon you during that time some speculations, and have only safeguarded myself in the title of this address by alluding to the functions of the fluid as possible rather than probable. As my colleague Professor Dixon is away on War service, I have had no opportunity of discussing the matter with him, so that if I say anything that is wildly improbable he at any rate is free from responsibility.

I shall dwell on the subject from the physiological rather than from

¹ Presidential Address delivered before the Neurological Section of the Royal Society of Medicine on October 26, 1916.

the pathological standpoint, but I trust that what I have to say will be found of interest to the pathologist and the clinical observer.

May I, after this preface, proceed to another chapter, which is also of a prefatory character, and state as shortly as I can the present state of our knowledge regarding the characters, composition and fate of the fluid. The fluid, as you know, is, under normal conditions, as clear as water and of low specific gravity; it contains in solution inorganic salts similar to those in the blood-plasma, a trace of coagulable protein, and a certain amount of a reducing substance which has now been definitely proved to be glucose; it is practically free from formed elements. Under various abnormal conditions the protein matter may be largely increased, or substances other than the usual ones may be added to it, such as cholesterol and choline (or a choline-like substance). It may further have added to it various kinds of cellular structures, the differentiation between which is a valuable aid in diagnosis, and in other cases parasites of different sorts may be found. The fluid is primarily formed by the secreting cells which are most prominently found covering the choroid plexuses in the cerebral ventricles, so that this structure may be appropriately designated, as Mott first suggested, the choroid gland. The fluid is normally present at a certain pressure, and this pressure is not the result of arterial pressure passively transmitted to the fluid. The cerebrospinal pressure, it is true, may be affected by changes in the arterial and venous pressures, but it is not dependent on them; and it may and often does vary quite independently of these. The true cerebrospinal pressure is the result of the secretory pressure of the choroid epithelium cells. In other words, the craniospinal contents cannot any longer be regarded as a fixed quantity without the power of expanding or contracting in volume.

The rate of flow and the pressure of the fluid can be readily investigated in animals by placing a cannula in the subcerebellar cisterna and connecting it with the necessary apparatus. It is then found that there are three groups of substances which promote the flow and increase the pressure independently of those which affect it secondarily by altering the blood-pressure. The first group consists of excess of carbon dioxide (or lack of oxygen) in the blood, as in asphyxia, and drugs which interfere with respiration. The second group is that of the volatile anæsthetics, which may act by interfering with the respiration or by altering the physical conditions of secretion. The third group is specific, and consists of an extract of the choroid gland, or of the brain. The former

is the more powerful. The chemical nature of the hormone in this extract is uncertain, but it is probably some product of nerve metabolism, which, arising in the brain, passes to the choroid plexuses, accumulates there, and stimulates the secreting cells to activity; it cannot be discovered in the normal secretion, but in cases of general paralysis and brain softening—conditions in which catabolic processes are excessive—it can be recognized (by physiological tests) in the fluid itself. The choroid plexuses are abundantly provided with nerves, but there is no evidence that these are secretory in nature; indeed the evidence derived from experiments with atropine and similar alkaloids points in the opposite direction. The hormone, whatever its nature, acts probably, not on nerves, but on the secreting cells directly.

There is no doubt that this fluid is being continually formed, and the next question is—What becomes of it? Large quantities of a neutral fluid, such as physiological saline solution, disappear within a few minutes when introduced into the craniovertebral cavity, and the course taken by such fluids, and presumably also of the normal cerebrospinal fluid, can be traced by adding some substance which can be easily recognized by its colour, or by chemical tests, or by its physiological action. Using such methods, it has been demonstrated that the exit is by the blood-stream, and not by the lymph channels of the nerves, which was formerly thought to be the case by a number of French observers.

If such substances are readily diffusible the speed with which they appear in the blood is very remarkable, especially if they are introduced into the subcerebellar region. An injection, for instance, of adrenaline, nicotine, or atropine produces typical physiological actions within a few seconds, in fact, almost as rapidly as if the injection had been made into the venous circulation direct.

On the other hand, substances which are not readily diffusible (such as commercial peptone) do not produce their characteristic effects when they are introduced into the cerebrospinal fluid, so that one of the older theories that actual valved orifices exist leading into the large veins at the base of the brain must be abandoned.

The diffusion process is most rapid in the subcerebellar district, but is extremely slow in the spinal, especially the lower spinal region.¹ It probably occurs into the venous sinuses by the microscopic arachnoid

¹ This is tacitly accepted by those who produce spinal anæsthesia by the injection intrathecally of substances of the cocaine group, for they recognize the danger of absorption if the drug reaches the medullary region.

villi described by Weed. There is also a possibility that in addition to this, transference may occur through the thin walls of the blood-vessels within the central nervous system, for, as Mott has pointed out, contact of these vessels with the cerebrospinal fluid is maintained throughout their extent by the perivascular spaces which are continuous with the subarachnoid cavity. Diffusion in the opposite direction from blood to cerebrospinal fluid does not occur except in an almost negligible degree in the case of a few drugs, such as alcohol and urethane.

But in addition to this there is another and minor communication between the fluid and the other parts of the body. Dixon and I found that dyes added to the fluid travel along the course of certain cranial nerves, and this is especially true for the olfactory nerve. This is not the case for the spinal nerves; no dye can be detected in their sheaths outside the spinal canal, and no dye is discernible in the lymph of the thoracic duct. I have spoken of this cranial (olfactory) outlet as a minor one, but clinical experience has shown that it is not a negligible one. For this loophole affords an opportunity for the entry of infective agents, as Flexner has shown in the causation of infective poliomyelitis.

Such then is a brief and I fear imperfect summary of the present state of our knowledge, and I propose now to pass to the main object of my address, which is to discuss the meaning and functions of the fluid we are dealing with.

In the first place it can hardly be doubted that the presence of fluid within and around the structures of the central nervous system fulfils certain mechanical functions of support and pressure. That, however, does not explain why ordinary lymph would not do just as well, as it does in the majority of other organs. The relationships, however, of the brain and cord within a closed cavity are peculiar, and it may be that ordinary lymph is here insufficient to maintain a more or less constant pressure. For the pressure of ordinary lymph is wholly dependent on blood-pressure; here, in addition, we have an independent pressure, namely, the secretory pressure of the choroidal secreting cells, and it is therefore quite possible that this may come into play in maintaining, equalizing, and adjusting those pressure relationships which are most advantageous for the well-being and function of the brain and cord. It is further quite possible that the ameliorative effects not infrequently noticed as a result of withdrawal of the cerebrospinal fluid by lumbar puncture may be due to the relief of undue pressure. But such

considerations offer no explanation of the peculiar composition of the fluid. Its characteristic chemical composition must have a deeper meaning.

It is very common to speak of the cerebrospinal fluid as the lymph of the brain. Let us now examine this phrase more fully, and see if it has any scientific accuracy.

In the first place we must be quite clear as to what lymph is, and what it does. It is a fluid which exudes through the thin walls of the blood capillaries. Whether lymph formation depends solely on physical conditions (filtration and osmosis), or whether in addition we have as a factor a secretory activity of the vascular lining membrane, is an interesting physiological problem, which need not concern us now. The leakage fluid resembles blood-plasma in its composition, except that it is comparatively poor in protein material, the diffusion of which through membranes is so difficult. This lymph, when formed, acts as the intermediary or middle-man between the blood and the tissue elements, conveying to the latter on the one hand the oxygen and nutritive substances they need; and on the other hand it is into the lymph primarily that the tissues pour the waste products of their activity, and thus these are started on their journey to the organs of excretion (lungs, kidneys, &c.). The very essence of a lymph is that it should be in free communication, except for an intervening membrane, with the blood-stream, and that this membrane should be equally permeable to water and other substances in both directions. The arrangement of the perivascular and perineuronal spaces, filled as they are with cerebrospinal fluid, certainly resembles that of a lymphatic system, and therefore it is not surprising that the idea has caught on that cerebrospinal fluid plays in the central nervous system the rôle of lymph. The peripheral nerves have a true lymphatic system analogous to that found in other organs, but anatomists are far from unanimous on the question whether the central nervous system possesses real lymphatic channels apart from the system of intercommunicating spaces occupied by cerebrospinal fluid. The mere difficulty of discovering true lymph-vessels does not indeed finally negative their existence, but until they are satisfactorily demonstrated we may provisionally assume that they are absent. If, then, cerebrospinal fluid is the only fluid which actually comes into contact with the tissue elements of the brain and cord, it necessarily follows that it must play the part played by lymph in other districts of the body; it must be for example the intermediary medium which is traversed by the oxygen on its way from blood to the tissue elements;

and oxygen we know is essential for the continuance of nervous life and energy. Furthermore it must be the vehicle by which other nutriment reaches the cells and fibres of nervous tissue. The next point is, have we any evidence that the products of nerve katabolism pass into the fluid from the tissue elements as they do into ordinary lymph? If it were only possible to analyse and compare the composition of the fluid before it enters the perineuronal spaces, and after it leaves them, it would be possible to answer this question authoritatively, but in the absence of such proof one can only argue from probabilities. Seeing that the fluid is the only one available for the purpose, an affirmative answer seems inevitable, and this is supported by the fact that cerebrospinal fluid is rich at any rate in one waste product—namely, carbon dioxide.

The expression "lymph of the brain" is therefore so far justifiable. But we have absolutely no proof that the cerebrospinal fluid is in part an exudation from the blood, and it is in the origin of the fluid that the analogy between lymph and cerebrospinal fluid breaks down. Whatever views we may hold as to whether a secretory factor comes into play in the production of ordinary lymph (and, at the best, such a factor can only be an insignificant one), we can have no hesitation in proclaiming that cerebrospinal fluid is a true secretion arising in a definite glandular structure. Such a fluid must obviously be the best one for maintaining normal life in the nerve cells, and the whole lining membrane of the spaces in which it resides appears to co-operate with the choroid gland in maintaining its constancy of composition, and to militate against the escape into it of substances from the blood-stream, such as drugs or poisons which would be foreign to the fluid or harmful to the delicate and sensitive structures which it bathes.

We have seen that the essential feature of a true lymph is the free interchange between it and the blood in both directions. This essential character is lacking in the cerebrospinal fluid; in all probability the lining membrane of the cerebrospinal spaces is permeable to substances passing from it into the blood, but it appears to be impermeable (except for oxygen) in the direction from the blood to the fluid. The nutritive materials the fluid contains appear to be formed in the choroid gland, and not to be merely exuded from the blood-stream; otherwise one cannot explain why the protein it contains is not similar to that in the blood or in exudations (lymph) formed from the blood.

If, as Weed has suggested, cerebrospinal fluid is partly formed, as ordinary lymph is, by exudation from the blood in the perivascular spaces,

it is difficult to understand why readily diffusible drugs and poisons do not escape readily into the cerebrospinal fluid as they do into ordinary lymph. The difficulty is quite intelligible when we regard the choroidal epithelium as a stalwart barrier of cells which keeps back these materials, and only allows its own normal secretion to escape. This useful work would be undermined and frustrated if the general lining were easily permeable to foreign substances.

Camus found that barium chloride, which is a very active poison to the central nervous system, will kill a rabbit of 2 kgr. weight when $\frac{1}{10}$ mgr. is introduced into the subarachnoid space, whereas the lethal dose is one thousand times greater when this salt is given subcutaneously. It is well known that anaphylaxis can be produced by smaller doses of proteins administered into the brain than when given elsewhere. The use of salvarsan in locomotor ataxy and similar late syphilitic affections *via* the cerebrospinal fluid has been abandoned, as it is fatal not only to the syphilitic organisms, but also to the patient. It is further known that salvarsan and its homologues are of little or no use in tabes and general paralysis when it is given by the ordinary channels, for in these later manifestations of syphilis the baneful spirochæte has got into a harbour of refuge (which we may speak of as extravascular) beyond the reach of the poison.

May I add in way of parenthesis how very desirable it is that chemists and pharmacologists should apply themselves to the solving of this difficulty. The future treatment of tabes and allied conditions should aim at the discovery of some blander arsenic compound which could be introduced straight into the cerebrospinal fluid and kill the syphilitic organism in its lair without at the same time slaying the host who harbours it.

Is not the very simplicity of the normal fluid suggestive? I remember when I was a student that normal or physiological saline solution was regarded as a physiological fetish, for surgeons continued to use sponges (usually dirty ones at that time) soaked in water during operations. What a change has now come over the spirit of their dream! They have realized that water, even clean water, is a protoplasmic poison, and that osmosis is a real force and not a negligible phenomenon. I remember, at about the same date, witnessing, and in a humble measure assisting, Dr. Sydney Ringer in his epoch-making work on the effects of saline mixtures on living structures. The attitude of the profession generally in those days was a tolerant one, just the sort of attitude adopted by a grandfather indulgently watching his descendants

playing with their toys. But who has not heard of Ringer's solution to-day? Who can write a paper on almost any physiological or pathological subject without mentioning it or alluding to the part it has played in his investigations?

Ringer's fluid is the ideal physiological salt solution; its saline constituents are present in the same proportion as they occur in the natural body fluids, and in that way the normal osmotic pressure is maintained when living structures are bathed in it. Ringer's original solution resembled frog's blood in its saline composition, but since then several modifications have been introduced. The most important of these is the one we owe to Locke, who has altered the proportion of the various salts (increasing, for example, the amount of sodium chloride from 0.6 to 0.9 per cent.), so that the fluid may be employed with success on the living tissues of the mammal. Locke has also added a small proportion of the sugar glucose, and when in use it is kept saturated with oxygen. It is well known that in such a fluid living structures can be preserved in a living condition for hours, or even days and weeks. Locke's most striking results have been obtained with the mammalian heart; this can be kept beating for prolonged periods after its complete isolation from the body if it is perfused with the oxygenated fluid. The salts supply the normal stimulus to the cardiac fibres and maintain their integrity; the sugar acts as a source of energy and is consumed as activity continues.

Ringer's fluid, so compounded in the laboratory, is somewhat more than thirty years old. But in reality it is as old as the hills, or rather as man himself. Just as the Venus of Milo existed potentially from past ages in the block of marble from which it was ultimately hewn, so does Ringer's fluid exist in the blood and lymph, although its simple composition is obscured there by admixture with the blood proteins and corpuscles.

Here may I introduce another parenthesis and allude to another physiological puzzle, and that is the significance of the large amount of protein in the blood plasma and lymph. The meaning and use of the blood corpuscles we understand, or at least we think we do, but the meaning of so large a quantity of protein in the blood fluid and the part it plays in nutrition is still hidden from us. The amount of protein necessary for the repair of the tissues is not great, and the modern doctrine of maintenance and growth is that the tissues help themselves, not from proteins directly, but from the various amino-acids which are the result of protein cleavage. The great protein store may be another

instance of the prodigality of Nature in providing a large margin for conditions of weakness and stress. However this may be, the presence of protein is not necessary, or it may even be harmful when it is added to Ringer's or Locke's solutions in experiments with perfused organs.

But to resume the thread of our argument. Thanks to Ringer some thirty years ago, physiologists were provided with a suitable fluid for experimental work, but the choroidal epithelium possessed the secret of extracting it from the blood for untold ages before Ringer was born. For what after all is cerebrospinal fluid but Locke's modification of Ringer's solution?

The view I have been led to take is—the nervous mechanism being so sensitive, so easily influenced by anything unusual—that therefore the neurons must be bathed in an ideal physiological saline solution to maintain their osmotic equilibrium; the trace of protein it contains is probably quite sufficient for nutritive processes, and is no doubt the kind of protein particularly suited to repair the small amount of wear and tear which is the result of nervous action. The sugar, just as in Locke's solution, would serve for a supply of energy. The choroidal epithelium, in its wise choice of a suitable circumambient medium for the neurons, is really exercising a protective function. In order to keep out harmful proteins (toxins and the like), the comparatively harmless ones are kept back also, almost completely; all share the same process of exclusion. This protective action applies in addition to the majority of soluble drugs; this, as we have seen, may operate so as to be detrimental in diseased conditions. But we can hardly expect discrimination on the part of the epithelial secreting cells. The non-access of metallic and other poisons to the nervous elements is such a *sine quâ non* for their health, that during those periods when such substances are given for the relief of disease, or the slaughtering of parasites, the choroidal cells are unable to change their habits and do not allow the drugs to get through.

Such I believe then is the real significance of the simple composition of this remarkable secretion. But before I sit down I must allude, in conclusion, to some other possible additional functions which the fluid may exercise.

The late Dr. Gaskell approached the question from the embryological and developmental point of view; he held that the neural tube represents an ancestral digestive canal, and those who adopt Gaskell's hypothesis might conceivably argue that the cerebrospinal fluid is the representative of a primitive digestive juice, and is secreted by an organ

which was formerly a digestive gland. However interesting such speculations may be, one can hardly suppose that anyone could seriously urge that the cerebrospinal fluid retains any such functions to-day.

Dendy is one of many comparative anatomists who have not accepted Gaskell's views, and he has suggested that the important function fulfilled by the choroid plexuses is that of an intracerebral gill, and is concerned in respiration. The structure of the plexuses is certainly gill-like, but it is always unwise to argue from mere anatomical resemblances. Mott, who analysed the gases of cerebrospinal fluid, found the quantity of carbon dioxide there very high (about 60 per cent.), and there is, therefore, something to be said in favour of the respiration hypothesis. It is quite possible that the choroidal epithelium may allow the escape of or even actively excrete this catabolic product, and it is unnecessary to point out how severe a poison any undue accumulation of carbon dioxide is in the central nervous system. Coupled with this fact is another I have previously mentioned—namely, that carbon dioxide is one of the most potent means of promoting a flow of the fluid. Just as urea is the best diuretic, and bile the best cholagogue, so carbon dioxide is one of the most powerful cerebral lymphagogues.

One further point and I have done. The ependyma is lined by ciliated epithelium. Some doubt exists, I believe, as to whether the cilia are functionally active. But if we admit they are, the question arises—In which direction do they act? This is a question which is hardly susceptible of actual observation in man or the higher animals, but in the *Amnocoetes*, which Professor Dendy has so largely used in his investigation, he has brought forward evidence which shows that the movement is in a forward direction. I know it is not always wise to draw conclusions from such lowly animals, and apply them without reserve to the higher ones. There are certain cases where such deductions are quite impossible, for instance, in some of the humble fishes the central canal of the spinal cord does not terminate blindly at its posterior extremity, but opens out by an orifice into the surrounding tissues.

In this case one can only speculate, and the rapidity of absorption of the fluid in the forward regions in comparison with that in the spinal district appears to favour Dendy's surmise. The cilia, if they are active, would no doubt further the flow of fluid from the cord region to the large veins at the base of the brain, where it so readily leaves the subarachnoid space by entering the venous blood-stream.

There are doubtless other problems in connection with the cerebrospinal fluid that demand solution, but my task is over. My main object has been to present the thesis in which I feel there is, at any rate, some truth—namely, to regard the cerebrospinal fluid as the perfect physiological medium, more perfect doubtless than the artificial fluids we can make in the laboratory, but in its essential features closely resembling those associated with the names of Ringer and Locke.

These are days of specialization, but however necessary specialization in medical science may be it has its attendant evils. Particularly regrettable is the divorce between those who pursue their investigations by the bedside and those who work in the laboratory. Neurology specially is a branch of our science in which an attempt should be made to bring about a closer *rapprochement* between the two sets of workers. Speaking personally I have derived inestimable benefit from hearing here the clinical side of the subject. Those responsible for the management of this Section of the Royal Society of Medicine have realized this, and in having elected this year a President who is a laboratory worker they have shown that they see the value of the *entente* I have alluded to; and I can only trust that my year of office may not be detrimental to those who form the larger contingent in the Neurological Section—namely, those who pursue more specially the study of disease by the bedside.

INTRACRANIAL ANEURYSMS.

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THE presence of a saccular aneurysm on one of the basal cerebral arteries at necropsy is one of the commonest pathological findings. Between 1907 and 1913 in the Pathological Institute of the London Hospital 7,924 *post-mortem* examinations of the body were made, in 5,432 of which an examination of the head was permitted, and saccular cerebral aneurysms were discovered in 44 cases. Osler [17] in his first 800 autopsies in Montreal found 12 instances, whilst Newton Pitt [16] in the dead-house of Guy's Hospital between the years 1869 and 1888 found 23 instances in nearly 9,000 examinations. In the past the chief causes of the formation of these aneurysms have been found in (i) embolism and (ii) syphilitic arteritis. In a recent paper entitled "Alterations in Arterial Structure and their Relation to Syphilis," H. M. Turnbull [24] has reviewed our knowledge as to the causations of aneurysms in general and of the morbid changes in the walls of the affected vessels. This paper, which is based upon the findings in the *post-mortem* room of the London Hospital during the years 1907 to 1913 inclusive, proves that the commonly accepted views as to the relation of intracranial aneurysm to an infection with the *Spirochæta pallida* are in need of revision.

CHAPTER I.—HISTORY.

The first definite account which I have been able to find of any intracranial aneurysm was published by Biumi of Milan in 1765, and was reprinted by Sandifort at Leyden in 1778; in this case an aneurysm of the internal carotid artery was found in a female of advanced age who had suffered from several severe rheumatic attacks. In 1814 Blackall in his work on "Dropsy" described an aneurysm of the basilar artery in a young female which had ruptured and produced fatal coma. Hodgson in the following year republished this case in detail and also described a second in which an aneurysm of the anterior cerebral artery, completely filled with blood-clot, was found at the *post-mortem* examination of the brain of an incurable lunatic who had been an in-patient for seventeen years at Bethlem Hospital; he referred to a third case, which had come under his notice, of a ruptured aneurysm of the size of a cherry on one of the cerebral arteries. In 1825 Spurgin of Saffron Walden published a case of aneurysm of the anterior cerebral artery, which occurred in a man of 57 who was suddenly seized with apoplectic symptoms; after a partial recovery and relapse he had a third fit in which he died. The aneurysm was about the size of a hazel-nut and had ruptured. In 1826 Serres published two cases; the first occurred in a man of 59 who died suddenly during convalescence from pneumonia; here, a ruptured aneurysm, of the size of a hen's egg, was found on the basilar artery. The second in a woman aged 53 who had suffered from epileptic seizures and was paralysed on the left side, where a bilocular ruptured aneurysm of the anterior communicating artery was found. Since this time records of cases of intracranial aneurysms are found scattered through medical literature. In 1834 Nebel first collected together and analysed the clinical findings in thirteen cases, and in 1836 Stumpff wrote a graduation thesis on fifteen cases. Brinton [5] in 1852, after describing a case of unruptured aneurysm of the anterior communicating artery, appended a table in which he gave statistical details of forty-nine cases. Gull [11] in 1859 entered more fully into the symptoms caused by aneurysms of the cerebral vessels and endeavoured to establish means by which they might be diagnosed during life, but concluded that "although we may from the circumstances sometimes suspect the presence of aneurysm within the cranium, we have at the best no symptoms upon which to ground more than a probable diagnosis."

The series of papers which Lebert [15] published in 1866 are

classical contributions to our knowledge of cerebral aneurysms. Lebert collected the records of 86 cases. He found that 47 of these had occurred on the carotid system of the arteries at the base of the brain and thirty-eight on the vertebral system, and that the incidence had been greatest on the middle cerebral arteries. Fifty-two of his cases had occurred in males and thirty in females; the arteries on the two halves of the body had been affected equally, except in the case of the internal carotid and posterior communicating arteries, where there was a preponderance on the left side. He first noted the frequency of the association of intracranial aneurysm with cardiac disease, but did not trace any causative relationship between these conditions. He gave an extremely lucid account of the clinical manifestations which had been observed in cases of cerebral aneurysm, and stated that in two-thirds of the cases of aneurysm of the middle cerebral arteries, and in 56 per cent. of all cases, rupture of the aneurysm had preceded and led to death. He correlated the common latency and exacerbation of symptoms with the liability of the aneurysms to partial ruptures. As to causes of cerebral aneurysms he considered mechanical, traumatic, and histological factors; in his opinion the majority were due to a "parenchymatous arteritis." "Calcifying atheroma is rarely found in cases of cerebral aneurysm and is not an important cause of their formation." He considered that the few cases which had occurred in patients giving a history of chronic alcoholism or of syphilitic infection did not support the hypothesis that these conditions bear any direct relationship to the formation of cerebral aneurysms. From his researches he was led to believe "that in a number of cases a definite diagnosis of cerebral aneurysm is possible."

Church [8] in 1870 first traced the causative relationship between the formation of intracranial aneurysms and vegetative endocarditis. Church was able to collect 13 cases, four of his own and nine from the literature, of cerebral aneurysms occurring in patients under 20 years of age due to emboli arising from endocarditic vegetations; these occurred on the right middle cerebral artery in 3 cases, on the left middle cerebral artery in 2 cases, on the basilar artery in 2 cases, on the posterior communicating artery in 2 cases, on the posterior cerebral in 1 case, on the right anterior cerebral in 1 case, on the left anterior cerebral in 1 case and on the left internal carotid in 1 case. At the end of his paper he stated that "further research has convinced me that intracranial aneurysms in the young are nearly always due to embolism."

Bartholow [1] in 1872, after reporting one new personally observed

and six newly collected cases, again reviewed the literature. From his studies of the records of 114 cases he concluded "there is much reason for believing that syphilis is the chief cause of the formation of intracranial aneurysms" and that after syphilitic aneurysms in order of frequency come those due to embolism from cardiac disease.

Ponfick [21] in 1873 clearly demonstrated the causative relationship between emboli and aneurysmal formation. The detailed description of the organs in his cases proves that all were examples of progressive, ulcerative endocarditis, but in the article of his paper he failed to recognize the infective nature of the emboli and attempted to explain the formation of the aneurysms on a mechanical basis.

Peacock [20] in 1876 analysed the pathological findings in cases of cerebral aneurysm. He reported 3 new cases and collected 86 from literature; he found that the internal carotid arteries had been affected in 12 cases, the anterior cerebral arteries in 4 cases, the anterior communicating arteries in 5 cases, the middle cerebral arteries in 27 cases, the vertebral arteries in 5 cases, the basilar arteries in 22 cases, the cerebellar arteries in three cases, and the posterior cerebral arteries in 6 cases. Death occurred from rupture of the sac in 17 of the 27 cases of aneurysm of the middle cerebral artery and in 14 of the 22 cases of aneurysm of the basilar artery. Of these aneurysms, 40 occurred on the left side and only 31 on the right, and 37 occurred in males and 43 in females. In Peacock's list no case of aneurysm of the posterior communicating artery appears, but, as Peacock notes, Bartholow in 1872 had already reported 8 such aneurysms. As to causation he remarks that "in some cases the disease seems to have originated in embolism" . . . "not infrequently the aneurysms seem to be caused by syphilis" . . . "the other cerebral arteries are often extensively diseased in cases of aneurysm, being thickened, atheromatous, and indurated, but in some cases the disease of the vessels is said to have been limited to the immediate seat of the aneurysm."

Eppinger [9], whose classical work on the pathology of aneurysms in general appeared in 1887, insisted that in the small and smallest arteries, like those forming the circle of Willis and its branches, many aneurysms have a congenital origin and are due to an inborn defect of the elastic properties of the arterial wall; in others congenital defects with subsequent degenerative or atheromatous processes complicating the defect are the essential factors in causation, whilst in a third group the aneurysms owe their origin to the local action of infective emboli, and in a fourth are due to local non-granulomatous inflammatory changes in the wall of the artery.

Newton Pitt [16], in his third Goulstonian Lecture delivered in 1890, gave an account of 23 cases of cerebral aneurysms which had occurred amongst nearly 9,000 patients who had been examined *post-mortem* at Guy's Hospital between the years 1869 and 1888. His main conclusions were: (1) It is most exceptional to find a cerebral aneurysm which is not associated with fungating endocarditis. (2) The lodging of a septic embolus is the starting point of the changes which take place in the vessel. (3) The clot inflames and in most cases disappears, the vessel dilating from the inflammatory changes in its coats. (4) An aneurysm may form and rupture in three weeks. (5) The onset of the embolism may not be marked by any symptoms, and the rupture of the aneurysm may be the first indication that there is danger.

In 1893 Gowers [10], in his manual of diseases of the nervous system, gave a general account and review of the subject of intracranial aneurysm and discussed the causes, general pathology, symptomatology, course, diagnosis and prognosis. Amongst causes he discussed (1) primary degeneration of the arterial walls, (2) injury, (3) syphilitic disease, (4) embolism. "Primary degeneration is an occasional cause in the second half of life . . . atheroma seldom leads to simple dilatation." With regard to syphilis he stated that "an aneurysm has been frequently met with in cases of constitutional syphilis in young adults, in whom no other cause of aneurysm was discoverable." "Embolism is probably the most frequent cause in the first half of life. There are few cases during this period, without indications of syphilis or injury, in which there is not evidence of past or present heart disease." He gave a list of the numerical frequency in 154 cases obtained by combining the statistics of various writers and found that there had been on the middle cerebral 44 cases, basilar 41, internal carotid 23, anterior cerebral 14, posterior communicating 8, anterior communicating 8, vertebral 7, posterior cerebral 6, and on the inferior cerebellar 3.

Von Hofmann [25] in 1894 published an account of the pathological changes and clinical manifestations which he had observed in 78 new cases of intracranial aneurysm. The order of frequency of affection of the various arteries in his cases was: (1) middle cerebral, (2) internal carotid, (3) anterior communicating, (4) basilar, (5) vertebral, (6) anterior cerebral. He found that the posterior communicating and posterior cerebral arteries had been only seldom affected, and did not find a single instance of a case of aneurysm of the cerebellar arteries. He observed that the favourite sites are (a) the bifurcations of the larger

vessels, and (b) the points of division of their branches. He discussed the relation of intracranial aneurysms to atheroma, syphilitic arteritis, embolism, and trauma, and concluded that neither atheroma, syphilis nor trauma are common direct causes of the formation of aneurysms; atheroma and a heightened-blood pressure are important factors in the causation of rupture, and the syphilitic endarteritis of Heubner may exceptionally give rise to aneurysmal formation. Of his cases 70 per cent. were females, and 30 per cent. were males. Fifty-eight were patients brought up to hospital by the police; 8 of these were found dead, 3 in the w.c., 2 in bed, 1 in a cellar, and 1 in a shop, and 8 others died before admission to hospital. He laid great stress upon the importance of looking for intracranial aneurysms in cases suspected of a violent death.

In 1901 Simmonds [23], following up the work of Ponfick and Eppinger, described the minute pathological and bacteriological features which he had found in seven cases of intracranial aneurysm due to infective emboli. All his cases were examples of progressive, malignant endocarditis where the septicæmia was of coccal origin; they occurred in children or young adults who at autopsy showed vegetations on the valvular endocardium and single aneurysms on the cerebral arteries, but no other abnormalities in the cardio-vascular system or changes in the kidneys.

Beadles [2] in 1907, in his Lecture before the Royal College of Surgeons, discussed the symptomatology of aneurysms of the larger cerebral arteries, basing his remarks on the notes of 555 cases of aneurysms of the cerebral arteries found after death, accounts of 441 of which had appeared in the literature and 114 were fresh material. At the end of the lecture he remarks that "notwithstanding the remarks made by some who have specially written on intracranial aneurysms and the writers of some of our leading text-books, the conclusion that I have been forced to draw from a careful study of a large series of cases is, therefore, that it is quite impossible to diagnose an aneurysm of any one of the cerebral arteries except in the most unusual circumstances. Only two or three have ever been diagnosed during life." "The apoplectic symptoms following rupture of an aneurysmal sac are indistinguishable from those of cerebral or meningeal hæmorrhage from other causes. If there is any one sign to which special attention might be drawn, it is the occasional intermittent character of the symptoms. But these form a very small proportion even of the cases where tumour symptoms were present, and, after all, it is not very

uncommon for symptoms to show variations in intensity, or even a temporary disappearance, in some other form of tumour and in other cerebral diseases."

The relative importance which, in recent years, authorities have placed upon the different factors which are known to be concerned with the formation of intracranial aneurysms have varied greatly. Thus in a clinical lecture delivered in 1908 John Rose Bradford [4] said: "The formation of a cerebral aneurysm is due to local disease of a vessel; it is a manifestation often of a patchy disease and not of a general arterial disease. . . . The local disease is, in a very large proportion of cases, atheroma, and is atheroma of no doubt syphilitic origin, and we think that in cases of cerebral aneurysms their causation by syphilis is, if anything, a more definite characteristic than it is even in such aneurysms as those of the aorta. In all the cases from which these specimens were removed where a history was obtainable there was no difficulty in tracing the syphilitic infection. . . . So much is that the case that you might make a more general statement and say that in aneurysms involving the larger vessels in young persons the probability of the condition being syphilitic is great. But bear in mind that in the case of the cerebral vessels, great as is the part played by syphilis, there is another factor which does not play any considerable part in the production of aneurysms elsewhere, that is the factor of embolism." Bruns [6], on the other hand, writing in the same year on the pathology of cerebral aneurysms, said that "in the majority of cases the aneurysms are due to arteriosclerosis and atheroma of the intima" and only admitted of syphilis as a cause of these underlying conditions.

Wichern [27] in two recent papers has reported the clinical histories and *post-mortem* findings in 22 new cases and has contributed to the better understanding of the clinical manifestations and to the diagnosis of the condition in patients suffering from aneurysms of the intracranial arteries. According to his analysis of his own cases, 5 were certainly and 3 probably of congenital origin, 5 were embolic, 2 were syphilitic, 2 occurred in patients suffering from general arteriosclerosis, and 2 were "atheromatous," but as far as can be judged from his paper Wichern uses the term "atheroma" to cover changes both in the intima and in the media of the arterial wall. In every one of Wichern's cases the aneurysmal sac had ruptured and in 15 of the 22 clinical or *post-mortem* evidence of previous leakage or rupture, on one or more occasions, was obtained. He insists that aneurysms of cerebral arteries are not rare

and that the infrequency of diagnosis in patients is due to the fact that the possibility of cerebral aneurysm as a diagnosis is rarely considered.

CHAPTER II.—THE PATHOLOGY OF INTRACRANIAL ANEURYSMS.

Turnbull [24] divides the chief abnormalities which affect the arteries into: (1) hypertrophies; (2) degenerations; (3) infiltrations; (4) inflammations, and (5) congenital malformations. He confines the term *inflammation* to reactions which are essentially active, and uses the term *degeneration* to distinguish those processes in which degeneration and necrosis are the primary and essential lesions. Only inflammations, degenerations and congenital structural malformations bear any causative relationship to the formation of intracranial aneurysms.

Atheroma is a degeneration which affects and is almost confined to the intima; it is found in both elastic and muscular arteries but is commoner in the large elastic; it is the result and not the cause of the increased blood-pressure which usually accompanies its presence; there is no evidence to be obtained in the *post-mortem* room to show that syphilis induces atheroma.

He finds that medial degenerations have the same cause as atheroma and may assume the forms of (a) fatty degeneration; (b) calcification associated with fatty degeneration; (c) mucous degeneration; (d) medial fibrosis.

In inflammations the arteries may be infected from their intima, either by micro-organisms settling upon the surface or by the arrest of infective emboli within their lumen. They may also be infected by micro-organisms reaching the media or adventitia by the vasa vasorum, or by direct inward spread of inflammation from the surrounding tissues. Inflammations of arteries may be divided into the *specific granulomatous inflammations* caused by syphilis, tuberculosis, rheumatism, &c., and *non-granulomatous* where the reaction is caused by the common pyogenic organisms. In his paper he separates for convenience of description the inflammations as they occur in the large elastic arteries, and in the muscular and small elastic arteries, and shows that acquired syphilis is far the commonest cause of aortitis, and is also the commonest cause of inflammation of the other large elastic arteries near the aorta, and, moreover, that syphilitic aortitis is the lesion of acquired syphilis which is found most frequently in

the *post-mortem* room of a General Hospital. In the small muscular and elastic arteries, the group to which the cerebral arteries belong, syphilis induces a relatively chronic arteritis, usually spoken of as endarteritis obliterans, in which changes in the intima are conspicuous and produce almost complete occlusion of the lumen. In the cerebral arteries, especially those of the base, arteritis consequent upon syphilis causes the artery to appear to naked-eye examination fusiform, white and thick, to feel firm and solid, and on transverse section to show a cut surface of firm, grey tissue, in the centre of which a minute red lumen may be visible. Microscopically, endarteritis obliterans is characterized by the appearance of an intimal thickening internal to the elastic lamina and the boundary stripe. In the earliest stages round cells are seen between the stripe and the endothelium. Spindle fibroblasts are found later and give rise to the formation of a definite granulation tissue. The granulation tissue ultimately becomes fibrotic and delicate elastic fibrils make their appearance. The elastic lamella and stripe remain unaltered throughout the process; this enables the condition to be recognized easily in sections stained by a specific method for demonstrating elastic tissue and to be distinguished readily from medial and intimal degeneration. The inflammation of the media and adventitia which accompanies the endarteritis conforms in type to the inflammation caused in other tissues by the particular micro-organism.

Turnbull discounts the use of the term *arterio-sclerosis* because it has been applied indiscriminately to hypertrophied arteries, to arteries showing atheromatous or (and) medial degeneration, to arteries infiltrated with amyloid, and to arteries reacting by inflammation. The term means merely "arterial hardening" and does not describe the pathological processes at work.

The term aneurysm (*ἀνευρίσσω*, widen or dilate) is used to describe any dilatation of an artery. In this paper, as in Turnbull's, however, we shall deal only with focal, true, fusiform or saccular aneurysms of a size large enough to be readily visible to the naked eye. *True aneurysms* are dilatations which are bounded by the coats of an artery. *False aneurysms*, on the other hand, are cavities which communicate with the lumen of an artery but are bounded by tissues external to the wall of the artery. True aneurysms frequently rupture and give rise secondarily to false aneurysms; the resulting structure is spoken of as a *mixed aneurysm*. In this paper, all false aneurysms in which there is evidence of a primary dilatation, that is to say, all mixed aneurysms,

will be referred to as true. The term "direct rupture" will be employed to denote a rupture which has not been preceded by aneurysm. False aneurysms will, therefore, be included among "direct ruptures."

According to Turnbull, true aneurysms thus described may be divided pathologically into two main groups: (1) *congenital*; (2) *acquired*. In the formation of acquired aneurysms generally, trauma, peptic digestion, inflammations, both granulomatous and non-granulomatous, degenerations, loss of mechanical support and heightened blood-pressure are the only known factors at work. Turnbull has not been able to find, either in the *post-mortem* room or from a study of the literature, any unequivocal evidence that aneurysms of the cerebral arteries are ever due to trauma; digestion by peptic ferments introduced from without and loss of mechanical support also cannot be assigned as important factors in the formation of intracranial aneurysms. The only factors which remain to be considered, therefore, are: (1) congenital; (2) inflammatory, and (3) degenerative.

In the series of cases which Turnbull and I have studied and which form the basis of this paper, no single example of granulomatous inflammation giving rise to a cerebral aneurysm occurred. Such cases, however, in the literature are not rare. They have been found most commonly on the vertebral and basilar system of the basal arteries and descriptions of their morbid characteristics have been given by many authors; Rose Bradford [3], for example, in 1894, showed a good example which occurred on the basilar artery in a patient who at autopsy also showed multiple gummata of the liver. Wichern [28] described two cases (Cases 19 and 20) of ruptured aneurysm of the basilar artery accompanied by diffuse syphilitic endarteritis obliterans of the cerebral vessels; the first was found in a widow of 56, who at autopsy also showed periostitis of the tibia and syphilitic mesaortitis, and the second in a woman of 51.

Unfortunately, as in the majority of my own cases, Wichern's patients were observed some years ago and before the recent development and application of the Wassermann technique, and so far I have not been able to find any more recently described case where the Wassermann reaction was tested both in the serum and in the cerebrospinal fluid *ante mortem* and where at autopsy an aneurysm of one of the cerebral vessels was discovered. In 1913, Langbein [14] published a description of a single case in which a positive Wassermann reaction in both the serum and in the cerebrospinal fluid was found in a man aged 40, which clinically simulated and which he himself

recorded as one of recurrent leakages on the part of a cerebral aneurysm; but the patient recovered and the nature of the meningitic affection and the cause of the recurring apoplectic attacks remain extremely doubtful, as no autopsy has as yet been performed.

The relatively high incidence of syphilitic aneurysm of the basilar artery is probably due to the fact that this artery is a large one and that in the smaller cerebral arteries syphilitic inflammation usually leads to such a severe degree of intimal hypertrophy that the lumen of the artery is blocked and thus prevents aneurysmal dilatation. When an extremely intense arteritis, whether granulomatous or non-granulomatous, affects the cerebral vessels, direct rupture or the formation of a false aneurysm may take place.

Aneurysms of the muscular and small elastic arteries frequently result from infection by bacteria which cause acute inflammations. The arteries are most commonly infected by impaction of emboli in their lumina. Aneurysms due to infective embolism are found most frequently in the cerebral arteries; the superior mesenteric artery is the second site of election. In our records they have occurred most frequently in cases of progressive malignant endocarditis. No aneurysms of cerebral vessels were caused by infection from without.

Saccular aneurysms due to medial degeneration, independent of inflammation, are found much more commonly on the cerebral arteries than on any other muscular arteries. In none of the cases of cerebral aneurysm which we have attributed to this class was there evidence at necropsy of active or healed endocarditis. In some there was evidence of cardio-vascular hypertrophy, accompanied by a considerable degree of general arterial degeneration, and in such cases, as Turnbull remarks, there would appear to be an adequate explanation of the formation of the aneurysms. In many of the cases, however, there was no evidence of excessive blood-pressure, either at autopsy or from clinical observations, and the general arterial degeneration and the degeneration of the cerebral arteries were no greater than in the average subject of the same age. In this respect many of the cases of aneurysm contrast sharply with the cases of direct rupture of central cerebral arteries. Direct rupture is usually associated with evidence of much more excessive blood-pressure (hyperpiesia) and arterial degeneration. There appears, therefore, to be an additional factor in the formation of cerebral aneurysms. This factor is, probably, (as Eppinger [9] first suggested) an inherent, inborn weakness due to a congenital abnormality in the structure of the arteries at their

points of junction and bifurcation. This conclusion is strengthened by the finding in the *post-mortem* room of the London Hospital in the year following the cases analysed in this paper of an aneurysm at the junction of the left anterior cerebral with the anterior communicating artery, in a child aged 1 year and 7 months, who died of broncho-pneumonia complicating acute gastro-enteritis.

The arteries of the brain all receive their blood from the internal carotid and vertebral arteries, whose anastomoses at the base of the brain form the arterial circle of Willis. On the ventral surface of the fore end of the medulla oblongata the two vertebral arteries unite to form the unpaired basilar artery; this artery courses over the pons and divides anteriorly into the two posterior cerebral arteries which run out almost at right angles to the parent vessel. The internal carotid arteries immediately after reaching the cranial cavity send back the posterior communicating arteries which unite the posterior cerebrals with the carotid system. On the side of the optic tract the internal carotid arteries give off the anterior cerebral arteries, which supply the frontal lobes and corpus callosum of the brain, and continue as the middle cerebral arteries. The two anterior cerebral arteries are united by the unpaired anterior communicating artery.

The circle of Willis is thus formed by :—

basilar artery	{	posterior cerebral—posterior communicating—	}	anterior communicating.
		posterior cerebral—posterior communicating—		
—carotid—	{	anterior cerebral	}	
—carotid—		anterior cerebral		

Although this is the “normal” arrangement, variations are extremely common. Amongst 200 successive observations on the conformation of the circle of Willis in dissecting-room subjects Windle [29] found that the number of arteries and their arrangement was “normal” in 119 (59·5 per cent.); the circle was symmetrical in 76, and symmetrical but for some inequality in size of the posterior communicating arteries in 43 others. In 159 the anterior communicating artery was normal; in 14 cases two anterior communicating arteries were present, in 1 case three were found, in 6 cases the artery was incompletely duplicated, in 6 cases the anterior cerebral arteries were united at their origin, in 2 cases both an union of the anterior cerebral arteries at their origin and also an ordinary anterior communicating artery were found, and in 9 cases a mesial artery arose from the anterior communicating artery. In 181 the anterior cerebral

arteries were normal; in 9 cases two anterior cerebral arteries were discovered with in addition a mesial artery arising from the anterior communicating artery; in 8 cases the anterior cerebrals were united for a distance and in 3 cases only a single mesial anterior cerebral artery was found. In 173 the posterior cerebral arteries and in 175 the posterior communicating arteries were normal. In size the posterior communicating arteries were often unequal, the right was larger than the left in 28 cases, and the left larger than the right in 15; both were small in 7 cases and both were absent in 3 cases; in 9 the right was absent and in 13 no left posterior communicating artery could be found. Wyrubow [30] amongst 112 successive examinations of the conformation of the circle of Willis in patients who had died from mental disease found that 22·3 per cent. showed abnormalities of the anterior cerebral arteries, and Parnisetti [19] at the autopsies on 87 criminals found only 51 (58·62 per cent.) with normal arrangements of the circle of Willis. Rothmann [22] states that in apes and anthropoids the anterior communicating artery is usually absent and the circle of Willis is thus not completed. Hofmann [13] found that the circle is usually incomplete anteriorly in frogs, salamanders and birds, and showed that amongst the various sub-groups of the mammalia the arrangements vary: zoologically closely related mammalia often show important differences in the arrangement of the basal cerebral arteries. Thus amongst the Ungulata, in the pig the circle is usually completed anteriorly; in the cow, on the other hand, this is not so. Amongst the Anthropoidea, in the gorilla no anterior communicating artery is found; in man this artery is normally present.

From these observations we see that morphological variations of a gross character are extremely common in the arteries forming the circle of Willis in all classes of the Vertebrata, and microscopical investigations have shown that minor changes in the elastic layer of the media of the arteries are also common in the cerebral arteries of patients who show no gross saccular aneurysmal dilatations. Most of the variations, whether major or minor, are found at the points of junction or of bifurcation of the vessels, and it is at these points that we find aneurysms visible to the naked eye of supposedly congenital origin.

In no case in this series of cases could any relation to trauma as a possible cause of the formation of intracranial aneurysm be traced.

Occurrence.—During the years 1907 to 1913 at the Pathological Institute of the London Hospital 7,924 *post-mortem* examinations of the body were made, in 5,432 of which an examination of the head was permitted. In these cases the following aneurysms were discovered:—

True Aneurysms of Aorta—

Due to syphilitic inflammation..	175
„ tuberculous inflammation	1
„ non-granulomatous inflammations	4
„ atheromatous degeneration	4
						184

Dissecting Aneurysms of Aorta—

Due to non-granulomatous inflammation	5
„ developmental deficiency	2
						7

True Aneurysms of Other Large Elastic Arteries—

Due to syphilitic inflammation..	43
----------------------------------	----	----	----	----	----	----

True Aneurysms of Muscular and Small Elastic Arteries (excluding the Cerebral Arteries)—

Due to syphilitic inflammation..	6
„ tuberculous inflammation (probably not all reported, most occur with pulmonary vomicae)	10
„ infective embolism	18
„ spread of inflammation from without	3
„ medial degeneration	7
						44

True Aneurysms of Cerebral Arteries—

Due to infective embolism	15
„ medial degeneration	36
						51

From this table we see that aneurysms of the aorta occurred in 191 cases or in 2·4 per cent. of examinations of the body, that 51 aneurysms of the cerebral arteries occurred in 44 cases or in 0·80 per cent. of examinations of the head, and that 44 aneurysms of the other large elastic arteries also occurred, i.e. one in 0·54 per cent. of examinations of the body. These figures contrast strongly with those from Crisp which Osler [17] quotes in his “System of Medicine,” where amongst 501 aneurysms, 184 occurred in the aorta, 137 in the popliteal artery and only 7 intracranial aneurysms were discovered.

The commonest cause of all aneurysms is syphilitic inflammation of the wall of an artery. Ninety-six per cent. (96·2 per cent.) of the aneurysms of the aorta, 100 per cent. of the aneurysms of the other large elastic arteries, but only 6·25 per cent. of the aneurysms of the muscular and small elastic arteries, to which class the arteries of the circle of Willis and the cerebral arteries generally belong, were consequent on the local weakening of the arterial wall due to the inflammatory reaction consequent on the activity of the *Spirochæta pallida*, and in no case in this series of necropsies was an intracranial aneurysm due to this cause found; at the same time the low rate of incidence of aneurysms on the vertebral system of arteries in this

series of cases, compared with those recorded by others, is extremely noteworthy.

In this series of examinations of the brain 31 cases showed thirty-six aneurysms of the cerebral arteries due to non-inflammatory medial change, and 13 cases showed fifteen cerebral aneurysms caused by infective embolism. Aneurysms due to non-inflammatory medial change occurred therefore in 0·55 per cent. of examinations of the brain, and aneurysms due to inflammatory changes in the cerebral arteries associated with infective embolism in 0·24 per cent.

Of these aneurysms on the cerebral arteries, death had been caused by rupture in 25 cases where the aneurysm was due to non-inflammatory changes, and in 10 cases where the aneurysm had resulted from infective embolism, or together in 4·42 per mille of the autopsies at the London Hospital during the years 1907 to 1913. During the same period intracranial hæmorrhage due to the direct rupture of central cerebral arteries consequent on medial degeneration was found in 72 cases or in 9·08 per mille of the autopsies, giving the relative frequency of cerebral hæmorrhages due to direct rupture compared with those following true aneurysmal formation of 35 to 72, or 1 to 2·05.

The following is a list of the sites of the cerebral aneurysms classified according to their pathological causes:—

	Embolic	Medial degeneration
Left intracranial carotid	1	1
Origin of cortical branch from left carotid	0	1
Junction right carotid with posterior communicans	0	1
Junction left carotid with posterior communicans.. .. .	0	2
Junction right carotid with middle cerebral	0	2
Right middle cerebral near base of brain	1	8
Left middle cerebral near base of brain	1	2
Cortical branches of right middle cerebral	4	2
Central branches of right middle cerebral.. .. .	0	1
Cortical branches of left middle cerebral	3	0
Central branches of left middle cerebral	1	0
Junction of right anterior cerebral with anterior communicans	0	2
Junction of left anterior cerebral with anterior communicans	0	7
Right anterior cerebral	2	2
Left anterior cerebral	1	1
Left anterior communicans	0	1
Junction of right posterior cerebral and posterior communicans	0	1
Bifurcation of basilar	1	0
Left posterior cerebellar branch of basilar.. .. .	0	1
Left anterior inferior cerebellar	0	1
	15	36

Multiple cerebral aneurysms due to medial change were found in four of the thirty-one cases:—

Case 3 showed two aneurysms on central branches of the right middle cerebral artery, one of which had ruptured.

Case 4 exhibited two intracranial aneurysms, one of which at the junction of the left anterior cerebral and the anterior communicating arteries had ruptured, and the other of which, at the junction of the right carotid and posterior communicating arteries was unruptured.

Case 11 showed two aneurysms, neither of which had ruptured; one of these was found on the right middle cerebral artery near the base of the brain, and the other at the junction of the left anterior cerebral and anterior communicating arteries.

Whilst Case 26 showed three aneurysms; one occurred at the junction of the left intracranial carotid and posterior communicating arteries and was ruptured, and the other two were found on the right middle cerebral artery and had not ruptured. Thus amongst 31 cases showing intracranial aneurysms, due to medial change, 4 cases exhibited nine aneurysms, and 31 cases thirty-six aneurysms.

Fifteen saccular aneurysms due to medial degeneration occurred at the actual point of junction of the arteries of the circle of Willis (Cases 4 (three examples), 5, 6, 8, 10, 11, 16, 17, 23, 24, 26, 27, 30). In addition, six were found close to such junctions and ten arose from the point of origin of branches. In two cases no note was made upon the relation to points of junction or bifurcation.

In one case two minute aneurysms were situated upon central cerebral branches. Of the remaining 34 due to medial degeneration, all except one sprang from cerebral arteries of the first order. Only three were connected with the posterior part of the circle of Willis.

The various sites of the intracranial aneurysms caused by infective embolism which occurred during the years 1907 to 1913 are given in the table on next page.

In this table are shown nineteen aneurysms of the muscular and small elastic arteries which occurred in 13 cases. Amongst these cases were found three aneurysms on visceral arteries and one on the profunda femoris artery. During the same period in cases where an examination of the head was permitted and no cerebral aneurysms were found, there occurred two aneurysms on the superior mesenteric artery, two on the splenic artery and one on the left brachial artery, giving the proportion of aneurysms due to infective embolism amongst 5,324 examinations of fifteen cerebral to nine on other arteries. In the 13 cases showing at autopsy cerebral aneurysms, ten of the cerebral

Number of cases	Right middle cerebral	Left middle cerebral	Branch on vertex right middle cerebral	Branch on vertex left middle cerebral	Right anterior cerebral	Left anterior cerebral	Left intra-cranial carotid	Bifurcation of basilar	Superior mesenteric	Celiac axis	Left renal artery	Left profunda femoris	—
4	R 4R	—	—	—	—	—	—	—	—	—	—	—	I, IV, VIII, X.
1	R	—	—	—	1R	1	—	—	—	—	—	—	II.
1	—	—	—	—	—	—	—	—	—	—	—	—	VI.
1	—	—	—	—	—	—	—	—	—	—	—	—	VII.
1	—	—	—	—	—	—	—	—	—	—	—	—	III.
1	—	—	—	—	—	—	—	—	—	—	—	1R	V.
1	—	—	—	—	—	—	1	—	—	—	1	—	IX.
1	—	—	—	—	—	—	—	—	1	—	—	—	XI.
1	—	—	—	—	—	—	—	—	—	—	—	—	XII.
1	—	—	—	—	—	—	—	—	—	—	—	—	XIII.
13	4	4	1	1	2	1	1	1	1	1	1	1	—
—	8R	4R	1R	—	2R	—	—	—	—	—	—	—	—

aneurysms and two of the other aneurysms had ruptured and given rise to considerable hæmorrhage. *Post-mortem* evidence of progressive malignant endocarditis was found in 10 of the cases; in 1 case a pyæmia subsequent to a retropharyngeal abscess, and in 1 case a pyæmia consequent on puerperal sepsis were found, and in 1 case the primary seat of the infection was not ascertained.

Multiple aneurysms due to emboli in cases of general septicæmia occurred in two cases.

Case V showed a ruptured aneurysm on a perforating branch of the left middle cerebral artery and an unruptured aneurysm on a cortical branch of the same artery; whilst Case XIII showed two ruptured cerebral aneurysms, one on a cortical branch of the left middle cerebral artery and a second on a cortical branch of the right anterior cerebral artery.

In 3 cases aneurysms on arteries in other parts of the body were also found.

Case V showed a ruptured aneurysm on the left profunda femoris artery; Case IX showed a ruptured aneurysm on the coeliac axis artery and an unruptured aneurysmal dilatation of the left renal artery; and Case XII an unruptured aneurysm on the superior mesenteric artery. Thus, of 13 cases 2 showed multiple intracranial aneurysms and 3 showed aneurysms of vessels in other parts of the body.

In this series of cases 17 intracranial aneurysms due to medial changes occurred on the left side, 19 on the right, whilst of those caused by infective embolism 7 were found on the left side and 7 on the right and 1 occurred at the bifurcation of the mesial basilar artery. Thus 24 occurred on the left half of the body and 26 on the right.

SIZE—

(a) Of Cerebral Aneurysms due to Medial Degeneration.

Smaller than a pin's head	Case 11	1
Size of a pin's head	Cases 10, 11, 21, 28 ..	4
Size of half-pea	Case 3	1
Size of a grape-stone	Case 26 (two examples) ..	2
Larger than a grape-stone	Case 26	1
Size of a pea	Cases 1, 3, 4, 4, 5, 6, 7, 12, 16, 20, 27, 29	12
Size of a cherry-stone	Cases 13, 15, 25	3
Size of a currant grape	Case 23	1
Size of a haricot-bean	Case 31	1
2 mm. in diameter	Case 2	1
3 mm. in diameter	Case 19	1
6 mm. in diameter	Cases 8, 17, 18 ..	3
14 mm. in diameter	Case 24	1
15 mm. by 10 mm.	Case 30	1
30 mm. in diameter	Case 14	1
No notes on size	Cases 9, 22	2

(b) Of Cerebral Aneurysms due to Infective Embolism.

Size of a pea	Cases II, V, VI	3
Size of a cherry-stone	Cases IV, VIII, X	3
Size of two peas	Case I	1
Size of three peas	Case III	1
Size of a cherry	Case VII	1
"Dilatation of vessel"	Cases V, IX, XI	3
25 mm. in diameter	Case XII	1
No notes on size	Case XIII (two examples)	2

15

Sex.—Cerebral aneurysms due to medial degeneration were found in 18 males and in 13 females, and due to infective emboli in 8 males and 5 females, giving a proportion in the whole series of cases of 26 males to 18 females.

Age.—If we divide up our cases of saccular aneurysms of cerebral arteries due to changes in the media according to the degree of cardio-vascular hypertrophy we find that:—

In two patients, aged 51 and 48, there was *very great* cardio-vascular hypertrophy.

In four patients, whose ages varied from 60 to 44, and averaged 50, there was *great* cardio-vascular hypertrophy.

In three patients, whose ages were 86, 75 and 50, there was *considerable* cardio-vascular hypertrophy.

In three patients, aged 55, 53 and 46, there was *moderate* cardio-vascular hypertrophy.

In three patients, aged 72, 67 and 60, there was *slight* cardio-vascular hypertrophy.

In fifteen patients, whose ages varied from 53 to 19 and averaged 38, there was *no* cardio-vascular hypertrophy.

And these cases were distributed between 50 and 54	2
" " " " 45 " 49	3
" " " " 40 " 44	4
" " " " 35 " 39	2
" " " " 30 " 34	0
" " " " 25 " 29	1
" " " " 20 " 24	2
" " " " 15 " 19	1

and in one case only an examination of the head was permitted.

A study of the incidence, therefore, in these thirty-one cases shows:—

That between the ages of 85 and 89 there occurred	1 case
" " 80 " 84 "	0 "
" " 75 " 79 "	1 "
" " 70 " 74 "	1 "
" " 65 " 69 "	1 "
" " 60 " 64 "	2 cases
" " 55 " 59 "	0 "
" " 50 " 54 "	6 "
" " 45 " 49 "	7 "
" " 40 " 44 "	6 "
" " 35 " 39 "	2 "
" " 30 " 34 "	0 "
" " 25 " 29 "	1 case
" " 20 " 24 "	2 cases
" " 15 " 19 "	1 case

The age-incidence of cerebral aneurysms of embolic origin is determined by that of chronic septicæmic and pyæmic conditions. In this series of cases

Between the ages of	5 and 9	there occurred	1 case
"	"	10 " 14	"	..	0 "
"	"	15 " 19	"	..	4 cases
"	"	20 " 24	"	..	3 "
"	"	25 " 29	"	..	0 "
"	"	30 " 34	"	..	1 case
"	"	35 " 39	"	..	2 cases
"	"	40 " 44	"	..	2 "
					—
					13
					—

CHAPTER III.—THE CLINICAL MANIFESTATIONS ASSOCIATED WITH INTRACRANIAL ANEURYSMS OF NON-EMBOLIC ORIGIN.

The course of illness and the actual manifestations of departure from healthy states which occur in patients who at autopsy exhibit aneurysmal dilatation *with rupture* of the larger cerebral arteries form a fairly definite nosological group. Nevertheless these deviations from the normal so closely resemble those seen in morbid intracranial conditions owing to other causes that Gull's statement written in 1859 still holds true "that although we may from the circumstances sometimes suspect the presence of an intracranial aneurysm, we have at the best no symptoms upon which to ground more than a probable diagnosis.

In nervous tissue, as contrasted with the other tissues of the body, function is more strictly localized. The interferences with function which result from the appearance of morbid changes in the vessels supplying the central nervous system depend upon the particular portions of the nervous axis which are affected secondarily. The finding on a given date of no single set of clinical manifestations of itself can enable us to pronounce a definite opinion upon the nature of the underlying pathological processes; tumour, syphilitic, and other forms of meningitis, aneurysm, &c., occurring at the same point, give rise to identical interferences, but for each the course of the disease is more or less characteristic, and if the possibility of aneurysm as a diagnosis were more frequently considered a larger number of cases would be recognized during life. In a considerable proportion of the cases which are included in this series a shrewd guess as to the causative factor was made before autopsy, and in a still larger number such a guess ought to have been hazarded. In the *post-mortem* room an aneurysm of one of the cerebral

arteries is a relatively common finding, and yet in the past when considering at the bedside the causative possibilities in a given patient cerebral aneurysms have rarely been suggested.

In 80·7 per cent. of the cases (25 out of 31) of non-embolic aneurysms due to changes in the media included in this series, signs attributable to cerebral hæmorrhage or to a local affection of the meninges consequent upon the *rupture* of the sac occurred, whilst in 16·1 per cent. (5 out of 31) an unruptured cerebral aneurysm, which, so far as is known, had not led during life to any definite manifestations, was found, and in 3·2 per cent. (1 case out of 31) in the history given by the patient on his admission to hospital was an account of a seizure and of an "influenzal" attack followed by much frontal headache and deafness of the right ear, which might or might not have been due to the development of an aneurysm at the junction of the right carotid and middle cerebral arteries.

Cerebral aneurysms which do *not* rupture rarely give rise to symptoms.

Death occurred in Case 7 from broncho-pneumonia consequent upon septic pharyngitis with abscess formation in the neck in a man aged 86, who five weeks previously awakened one morning complaining of an inability to utter words. At the autopsy atheroma of most of the cerebral arteries and unruptured aneurysm, of the size of a pea, was found on the right middle cerebral artery near the base of the brain. In Case 8 the patient, a man aged 75, died forty hours after a suprapubic prostatectomy and an unsuspected and unruptured aneurysm, 6 mm. in diameter, was found at the junction of the left anterior cerebral and anterior communicating arteries. Case 11, a fish-curer, aged 53, for two and a half years before death suffered from hæmaturia and renal insufficiency associated with congenital cystic kidneys. He died "uræmic," and at autopsy two small unruptured aneurysms were found, one at the junction of the left anterior cerebral and anterior communicating arteries, of the size of a pin's head, and the other, rather smaller, on the right middle cerebral artery near the base of the brain.

Case 19 was that of a married woman aged 48; for five years she had suffered from symptoms attributable to cholelithiasis, and eighteen days before death was admitted to hospital with an acute surgical condition of the abdomen. Laparotomy was immediately performed; a tumour of the gall-bladder was removed and a subphrenic abscess drained. After the operation her general condition grew worse, hæmatemesis from acute ulceration of the stomach set in and she died of

internal hæmorrhage. At the autopsy an unruptured aneurysm on the right middle cerebral artery, 3 mm. in diameter, was found near the base of the brain. Case 21 was admitted to hospital with symptoms of Korsakow's psychosis and alcoholic peripheral neuritis, from which she died. At autopsy cirrhosis of the liver, fibrosis of the pancreas and a certain degree of cirrhosis of the kidneys, and in addition an unruptured aneurysm, of the size of a pin's head, on the left middle cerebral artery about 1 in. from its origin, were found.

Case 20 is our only example of a patient in whom an unruptured aneurysm at the time of its development probably caused certain intracranial disturbances which came on acutely and then remained quiescent until the death of the patient from an intercurrent disease bearing no direct relation to the vascular system. This man, when aged 47, was admitted to hospital with signs of acute diffuse myelitis from which he died. He gave the history that six years before death he had suffered a slight seizure followed by general weakness, irritability and depression, and that about a year previously he had had an attack of "influenza" followed by deafness of the right ear and much frontal headache. Here an unruptured aneurysm, of the size of a large pea, was found at the junction of the right carotid and middle cerebral arteries, in addition to diffuse inflammation of the spinal cord.

Two of the patients included in this series *died before admission to hospital*. Of the previous history of Case 1 nothing is known. The patient, a man aged about 51, was found by the police lying dead in the street; a ruptured aneurysm of the size of a pea was found on the right middle cerebral artery near the base of the brain. The case was one of hyperpiesia; atheroma was present in the wall of the aneurysm, in most of the cerebral arteries and in most of the systemic arteries, and the heart showed left-sided hypertrophy. Case 28 was that of a clerk, aged 22, who had gained some local fame as a cyclist; after riding a mile at a public cycle-race meeting he "came over giddy," got off his machine, lay down on the side of the track, lost consciousness almost immediately and died within half an hour of the onset of the symptoms. At the autopsy a ruptured aneurysm on the right middle cerebral artery, 4 cm. from its origin and near the base of the brain, of the size of a pin's head, was discovered; in the rest of the cardiovascular system no gross changes were found.

Ten cases were admitted *after a first apoplectic seizure, and died without ever recovering consciousness*. Case 9, a man aged about 50, lived only one hour and a half after his admission; in this case the

diagnosis of "fractured base" was made owing to the history of a fall in the street and the finding on examination of a bruise on the occiput. At the *post-mortem* examination a ruptured aneurysm was found on the right anterior cerebral artery just beyond the origin of the anterior communicating artery: and in the great longitudinal fissure old altered blood-clot and staining of the meninges was present, suggesting that a partial rupture had occurred on some previous occasion.

Case 10 was that of a greengrocer, aged 55; he, too, was found lying in the street by the police and died in coma about an hour after admission. This patient showed left hemiplegia, unequal fixed pupils—the right larger than the left—hyperpiesia and enlargement of the left ventricle. At the autopsy a ruptured aneurysm of the size of a pin's head was found at the junction of the right anterior cerebral and anterior communicating arteries.

Case 24 died unconscious within a few hours after admission. The patient was a woman hawker, aged 40, who was found by the police lying stertorous and deeply cyanosed on the roadside. On admission, both pupils were widely dilated, and neither reacted to light, and both plantar reflexes gave an extensor response. Here the ruptured aneurysm, 1.4 cm. in diameter, was found at the junction of the right posterior cerebral and posterior communicating arteries.

Case 18 was that of a married woman, aged 49, who was said to have suffered for four months from nocturnal frequency of micturition, occasional attacks of headache, and a general nervous state of irritability attributed to the onset of the menopause. Eight days before death an extremely severe attack of headache leading to nausea and vomiting was complained of; the headache persisted for six days, and then the patient became delirious and lost consciousness. On admission ten hours before death she was deeply unconscious, and no local signs of interference with motion or with the functions of the cranial nerves were discovered. Two hours after admission she exhibited three generalized convulsions, developed hyperpyrexia ($T. = 106^{\circ} F.$), and died. The aneurysm, which had ruptured, was found on the left anterior communicating artery, and was 6 mm. in diameter; there were few signs of cardiovascular disease.

Case 27, a compositor, single, aged 28, had suffered for eighteen months from attacks of left-sided headache, accompanied during the last six months by severe nausea and giddiness, and usually some vomiting; sixteen hours before death he got up in the morning feeling

particularly well, and went to the bathroom, where he fainted and lost consciousness. Fourteen hours after this seizure he was admitted moribund, and within ninety minutes died with increasing coma and cyanosis. An aneurysm, of the size of a pea, which had ruptured, was found on the left intracranial carotid artery at the origin of a branch to the temporal pole. The rest of the cardio-vascular system showed few signs of disease.

Case 17 was that of a labourer, aged 51, who had been addicted to alcoholic excess, and for several winters subject to attacks of "winter-cough." About a month before death manifestations of cardiac failure appeared without any symptoms referable to the nervous system. Eighteen hours before death he was seized with a sudden intense headache, leading to vomiting and the appearance of a right-sided extensor plantar response; he lost consciousness, and died eighteen hours later. A ruptured aneurysm, 6 mm. in diameter, was found at the *post-mortem* examination on the left anterior communicating artery.

Case 13, an old woman, aged 72, who lived alone, was found lying unconscious in her kitchen; she died twenty-eight hours later. On admission neither pupil reacted to light, and both plantar reflexes gave an extensor response. An aneurysm, of the size of a cherry-stone, which had burst, was found on the left anterior cerebral artery just beyond the origin of the left anterior communicating artery. In this case there was moderate general arterial degeneration and moderate cardio-vascular hypertrophy.

A married woman, aged 48 (Case 2), was suddenly seized with apoplexy whilst in the street, and died unconscious thirty-six hours later. In this case widespread cardio-vascular changes were found at the autopsy, together with a ruptured aneurysm, 2 mm. in diameter, on the right middle cerebral artery near the base of the brain.

Case 5 was that of a man, aged 49, a painter by trade, who, whilst at work in the hospital garden, fell, and was found later lying unconscious. He was admitted immediately, but never recovered consciousness; he died on the third day after the seizure of respiratory failure. Lumbar puncture in this case showed the presence of much free blood in the cerebrospinal fluid, and the examination of the patient revealed general vascular disease, hyperpiesia, right facial paresis, and evidence of bilateral corticospinal interference. At the autopsy atheroma of most of the cerebral vessels, general arterial degeneration and hypertrophy of the left ventricle were found, and also a ruptured aneurysm of the size of a pea at the junction of the left anterior cerebral and anterior communicating arteries.

In Case 6 the patient, a married woman, aged 44, had suffered for several years from "ill-health, depression, and hysterical fits"; for these she took alcohol to excess. Twenty-four days before death she began to complain of severe pain in the head, acute diarrhoea, and much vomiting; this attack lasted three days. Then she improved somewhat, but remained drowsy, and talked irrationally. Fourteen days before death she was admitted to hospital in a drowsy, apathetic, lethargic state, passing urine and faeces under her. On examination, the calves were exquisitely tender to pressure, the knee-jerks and ankle-jerks were abolished, but the left plantar response was extensor; from time to time the patient showed attacks of irregular movements of the right upper extremity. In this state she remained for several days, then signs of broncho-pneumonia developed, and she died. The autopsy showed a ruptured aneurysm of the size of a pea at the junction of the left anterior cerebral and anterior communicating arteries, whilst both anterior cerebral arteries arose from the left internal carotid. All the cerebral and most of the systemic arteries showed medial and atheromatous changes, and the left ventricle was much enlarged.

The clinical history in this case, although the patient never regained complete consciousness after her first seizure, forms a connecting link with the more definite and more easily recognized group of cases in which multiple seizures at varying intervals and signs of localized interferences at the base of the brain precede the fatal issue.

When death in a case of ruptured cerebral aneurysm follows directly upon the first rupture of the sac, the differential diagnosis between intracerebral and intrameningeal hæmorrhage can only be made after a full consideration of all the attendant *localizing* symptoms and signs; and these often are insufficient to lead to the formation of a correct opinion. In 41·9 per cent. of cases (13 out of 31) of cerebral aneurysms of non-embolic origin in this series, however, an especial feature, which, so far as my experience goes, amongst all other intracranial conditions is characteristic of ruptures of this class of aneurysms, was also present, viz.: an account in the history of the patient's manifestations of a sudden exacerbation, with apoplectiform onset, of symptoms and signs followed by a period of varying, but often considerable, duration, in which no fresh developments appeared, followed later by a second and a third, and even by a fourth, seizure, in the last of which death from respiratory failure and medullary pressure occurred, and correlated with this the finding at autopsy of

evidence of leakages of different ages owing to partial ruptures of the aneurysmal sac.

Wichern [27 and 28], from a study of the literature of cerebral aneurysms in general, found that multiple seizures had occurred in 57 out of 183 cases (31.1 per cent.), figures which correspond well with the 13 out of 44 cases (29.6 per cent.) of all classes of cerebral aneurysms which, on the one hand, manifested multiple seizures, and, on the other, were examined in the *post-mortem* room of the London Hospital during the period under consideration.

A case of aneurysm at the junction of the left internal carotid and posterior communicating arteries of congenital origin which first give rise to symptoms at the age of 19. Three partial ruptures giving rise to apoplecticiform attacks. Admitted to hospital showing complete paralysis of the left third cranial nerve, optic neuritis on left and proptosis on right, and left cerebellar posture of head. Cerebrospinal fluid blood stained. Death from respiratory failure twenty-four days after onset of manifestations.

Case 30.—31256/1911. Arthur F., aged 19, painter, single, was admitted to the London Hospital, under the care of Dr. W. J. Hadley, on June 8, and died on June 24, 1911.

Until June 1, 1911, the health of this patient had been uniformly good. On the afternoon of that day, whilst at work, he was suddenly seized with acute pain in the head "as if the head would burst" and "a feeling of stiffness all down the left side of the neck." The headache led to vomiting; the vomiting did not relieve the pain nor the feeling of stiffness. He lay down for about two hours, when the headache became less severe. He was then able to walk the quarter of a mile from his work to his home. On the next day he still suffered from severe headache over the left half of his forehead and down the left side of his neck. On June 3 he got up but did not go to work; on this day the headache, though still present, was less severe. On June 4, the pains in his head again became more severe and his appetite failed. On June 5 the headache was still severe and he experienced difficulty in opening his left eye. On the morning of June 6 he was totally unable to open his left eye. On June 7 and 8 the headache was constant and severe. On June 8 he first sought medical advice; he was seen as an out-patient by Dr. Lewis Smith and admitted to hospital.

The patient was the second of four children: his two brothers and sisters were healthy and his father and mother were alive and healthy. As a child and young man his health had been good. The only illness he remembered was an attack of scarlet fever at the age of 10 years. He denied all venereal infection and all exposure. Previous to the onset of the illness for which he was admitted he had never suffered from headache.

The patient was a well-developed healthy-looking young man of 19. He

weighed 6 st. 11½ lb. He was drowsy and lethargic and only spoke when addressed. Speech was unaffected. Before June, 1911, he had never suffered from fits or other forms of seizure. He complained of a severe headache confined to the left half of his head and neck, "a dull, constant, heavy feeling, varying a little in intensity from time to time." The left side of his head was tender on pressure: the tenderness extended down over the left mastoid region and was general. Vomiting had occurred on June 1.

With the right eye the patient could see distant objects with fair ease, but with this eye he was unable to read the newspaper. Vision with the left eye was unimpaired. The arteries of the right fundus appeared normal, but the veins were engorged, whilst the disc appeared healthy; on this side there was some œdema of the lower quadrants of the fundus. On admission, the left fundus was not clearly seen, but in it no gross change was detected. Hearing, smell and taste were unaffected.

The left upper eyelid could not be raised, and of the muscles moving the left eyeball only the external rectus was not paralysed. The right eyeball was prominent but its movements were unimpaired. The right pupil was of moderate size and reacted readily to light and on accommodation. The left pupil was widely dilated and did not react either to light or to attempts at accommodation. The action of the muscles moving the jaws was normal. The right side of the face was flat and the nasolabial fold was more prominent on the left side than on the right, but in voluntary and emotional movements the face moved naturally. The movements of the palate and larynx were unimpaired. The tongue could be protruded straight and held steadily.

He walked naturally; gait was unaffected and Romberg's sign was not obtained. Whilst lying in bed he habitually held his head flexed towards the left with the chin pointing to the right. The muscles of the left side of the neck were in constant spasm. The grasps were powerful and co-ordination of the hands and legs was unimpaired. No anæsthesia or alteration in sensibility could be discovered to testing with the prick of a pin, cotton wool, the hot and cold tubes and for postures and passive movements.

The knee-jerks were readily obtained and about equal on the two sides. Ankle-clonus was not present and the arm-jerks were normal. The abdominal reflexes were readily elicited and both plantar reflexes gave a flexor response. The sphincters were under control.

The apex-beat of the heart was felt in the fifth space 2½ in. from the mid-sternal line. The area of cardiac dulness was not increased. The heart sounds were pure. The rate of the pulse varied from 76 to 90 per minute and that of respiration from 20 to 24 per minute. No abnormal signs were found over the lungs. The temperature on admission was 100° F.; throughout the patient's stay in hospital the temperature oscillated in an irregular manner between 97° and 100° F. No abnormal signs were discovered in the abdomen; the liver and spleen could not be felt. The quantity of urine passed in twenty-four hours varied from 50 to 80 oz., the specific gravity from 1014 to 1028; neither albumen nor sugar was ever found. There was no glandular enlargement.

During the whole period of observation headache was a constant feature and was not affected by the administration of drugs. The pains in the left cervical region gradually spread down the spine as far as the lumbar region, but this spread was not accompanied by any exacerbation in the headache. On June 15, the prominence of the right eye, noted on admission, became more definite and was now associated with lateral nystagmus both to the right and to the left and with coarse hippus of the pupil of the right eye; on this day, too, Kernig's sign was readily elicited on both sides.

On June 15, and again on June 18, lumbar puncture was performed; on each occasion blood-stained fluid escaped at considerable pressure, and it was observed that the longer the cerebrospinal fluid ran the more blood the specimen obtained contained.

On the morning of June 24, five hours before death, the patient's condition was closely similar to that seen on admission. He was, however, more irritable and mentally more dull than he had been on the previous four or five days. The neck muscles on both sides were rigid and the patient deeply resented all passive movements of his neck. The grasps were feeble. All the limb muscles were hypotonic but there was no absolute paralysis. The knee- and ankle-jerks could not be obtained. Both plantar reflexes gave a flexor response and the abdominal reflexes were readily elicited, and equal on the two sides. Kernig's sign was still present in both legs. On the left side the fundal veins were distended, the arteries were small and difficult to see, and the whole fundus appeared hazy; the edges of the disc were blurred and oedematous; the swelling measured more than 1 and less than 2 D.; no hæmorrhages were seen. On the right the veins were full, the arteries normal, and except for some slight blurring of the inferior and temporal quadrant the edges of the disc clear. All movements of the right eye were normal. The left third cranial nerve was completely paralysed. The left pupil was widely dilated and did not react to stimulation with intense light, the right pupil was small or of moderate size in dull light, and reacted sluggishly to intense light and doubtfully also on accommodation. The lower half of the right side of the face was paretic. The other cranial nerves were unaffected. The blood-pressure by Riva Rocci apparatus in the right brachial artery was 110 mm., in the right leg 114 mm., and in the left brachial artery 109 mm.

On June 21 the patient had had a slight convulsive seizure lasting about twenty seconds, during which time urine was voided. About 12.50 p.m., on June 24, the patient was observed to have developed stertor; no movements occurred. Five minutes later on examination he showed ptosis of both eyes of about equal severity and a bilateral divergent strabismus. The left pupil was dilated and fixed, the right of pin-point size and also fixed. Both arms and both legs were flaccid. The left knee-jerk was readily elicited, whilst the right could not be obtained, and both plantar reflexes gave a flexor response.

Three minutes later (12.58 p.m.), both arms were stiff, the right more so than the left. A knee-clonus was readily elicited on both sides, and both plantar reflexes gave an extensor response. By this time the breathing was

regular and deep. At 1.1 p.m. stertor again developed and was accompanied by flexor-extensor movements of the right half of the body and of the right arm and right leg. The drooping of the upper eyelids previously noticed disappeared and the right eyeball now looked directly forwards, whilst the left still deviated outwards. Lumbar puncture was now performed (1.5 p.m.) and two test tubes full of deeply blood-stained fluid obtained. For a time this procedure seemed to give relief, but at 1.30 p.m. stertor again set in and the patient became cyanosed. For the first time since admission the palpebral fissures were now equal, but the visual axes of both eyeballs deviated widely temporal-wards. The pulse was small and thready. Gradually respiration failed, the respiratory movements becoming more and more feeble and shallow in spite of the administration of oxygen. The heart was heard beating ten minutes after all apparent respiratory movements had ceased. Artificial respiration was begun, but death occurred at 2 p.m.

At the *post-mortem* examination, which took place on June 25 (P.M. 583/1911), an aneurysm measuring 1.5 cm. by 1 cm. was found at the junction of the left internal carotid and left posterior communicating arteries. This aneurysm had ruptured and a mass of blood-clot measuring 3 cm. in diameter was found over the anterior and internal subjacent portion of the left temporo-sphenoidal lobe. The meninges around the circle of Willis, more especially in the posterior fossa, were densely matted. The left third cranial nerve was stretched over and was adherent to the posterior extremity of the aneurysm. The lepto-meninges everywhere were stained brown. The lateral ventricle on both sides contained recent red clot and the surfaces of the spinal cord, more especially the posterior, were covered with dark red blood-clot. The brain weighed 1,403 gm.

The cerebral arteries appeared healthy. The heart weighed 269 gm. The valves appeared healthy; on the pericardium a few milk-spots were seen. A few fatty streaks were seen in the lower thoracic and in the abdominal aorta and at the bifurcation of the common carotid artery. The crypts of the tonsils contained muco-pus and each tonsil measured 2.3 cm. in diameter. The liver, lungs, and kidneys were congested. In the left kidney a small congenital cyst was found, and on the surface of the spleen was a small patch of perisplenitis. A small calcareo-caseous nodule was present in one of the caecal glands.

Thus, apart from the cerebral aneurysm which had ruptured and caused death, all the organs appeared healthy. There were no signs of any cardiovascular hypertrophy, of old or recent endocarditis, and nothing to suggest any syphilitic infection.

A case of death from cerebral hæmorrhage which showed at autopsy a ruptured aneurysm at the junction of the left anterior cerebral and anterior communicating arteries and an unruptured aneurysm at the junction of the right carotid and posterior communicating arteries, with great cardiovascular hypertrophy, general arterial degeneration and atheroma of the cerebral

arteries, in which manifestations of intracranial disorder first occurred at the age of 47. Three apoplectiform attacks preceded the fatal issue. Headache, noises in the head, double optic neuritis, paralysis of the left external rectus, ptosis left. Death from respiratory failure fifty days after the onset of acute symptoms.

Case 4.—43036/07, Matilda H., married, aged 49, was admitted to the London Hospital under the care of Dr. Francis Warner on December 14, 1907, and died on December 30.

Until 1905 her health had been good, but about two years before her death "family matters went wrong," she began to worry, became subject to attacks of severe frontal headache and suffered greatly from noises in the head and sleeplessness. In the months preceding her admission the headaches had been more frequent, more persistent and more severe. On the afternoon of November 10, 1907, fifty days before death, whilst sitting at home in her kitchen she had a "seizure"; the attack came on suddenly; "a feeling of fullness came before my eyes and was then followed by a splitting headache and severe giddiness; my sight became dim and misty, and everything looked indistinct and far away." She did not completely lose consciousness nor did she vomit. During the attack she was able to move her limbs naturally and at will, and could understand what the people around her were saying. The "seizure" lasted about five minutes; it was followed by a feeling of lassitude and inability to stir, which lasted until bed-time but did not prevent her carrying out her household duties. On the morning of the 11th she got up at the usual time and prepared breakfast, but complained of severe vertical headache; this headache persisted for three days. On November 13 she began to see double, and it was noticed that her left upper eyelid drooped; but at this time her limbs were not affected. On the 14th, four days after the seizure, she did the weekly washing for the household.

Two weeks later, on November 28, whilst at work in the washhouse, "a feeling of giddiness seized me; I sat down on a chair, then I completely lost myself and fell on to the floor; when I came to myself I was in bed; then I vomited incessantly for several days; the vomiting bore no relation to the intake of food and did not relieve the headache." She stayed in bed for twelve days. When she got up her memory for recent events, for instance as to where she had put her purse or placed things about the house, had become extremely bad. From that time until admission she complained of a constant severe headache located at the back of the eyes and over the vertex, of diplopia for distant objects, and of a dislike for bright lights. The headache was worse when the patient lay recumbent; it did not prevent sleep and was always worse shortly after waking. The ptosis of the left eye persisted unchanged.

The patient was a married woman of 49; her periods had been irregular for the six months preceding admission. Her husband, aged 51, was alive and, except that he was subject to attacks of acute gout, healthy. Her father, aged 85, was living and healthy; her mother died at the age of 65 from "asthma and bronchitis." She was the fourth of six children, her three brothers and two

sisters were alive and healthy. She married at the age of 18 and had had fourteen children and two miscarriages: (i) male, living and healthy, aged 30; (ii) miscarriage at five months; (iii) female, living and healthy, aged 28; (iv) male, living and healthy, aged 26; (v) full-time child, born dead; (vi) male, living and healthy, aged 24; (vii) male, living and healthy, aged 23; (viii) male, lived three days; (ix) male, living and healthy, aged 21; (x) female, died, aged 2; (xi) female, living and healthy, aged 15; (xii) male, died, aged 1 $\frac{3}{4}$; (xiii) female, living and healthy, aged 12; (xiv) miscarriage of twins at 3 $\frac{1}{2}$ months; (xv) male, living and healthy, aged 10; (xvi) female, died, aged 8 months, of "wasting." There was no history suggestive of venereal infection.

The patient was a well-covered woman of healthy appearance. Mentally she was dull and apathetic. Speech was unaffected. Memory for past events was clear and she gave her history in clear, lucid terms; she volunteered the information, however, that her memory for recent events was poor. She suffered neither from hallucinations nor delusions. She complained of a constant severe headache at the back of the eyes and over the vertex, which was most severe on waking and in the early morning. The headache did not extend into the neck or temporal regions and was not accompanied by pressure or percussion tenderness of the skull. She complained of a constant feeling of sickness which occasionally led to actual vomiting; the vomiting did not relieve the headache or the nausea, and bore no relation to the intake of food.

There was no paralysis of any limb, and to tests no alteration in sensibility could be discovered.

The knee-jerks were readily elicited and equal; ankle-clonus was not obtained. The deep reflexes of the upper extremities were normal. On each side stimulation of the sole of the foot gave rise to a brisk response; the first response was usually extensor, but then the toes would flex.

The left palpebral fissure was narrower than the right, and the left upper eyelid could not be raised voluntarily. For objects at a greater distance than 18 in. from the eyes, double vision occurred, for nearer objects single vision. The right external rectus was paralysed; all the other muscles moving the eyeballs acted normally and nystagmus was not present. The pupils were equal and reacted well both to light and to accommodation. There was some evidence of left facial paresis; the left nasolabial fold was less definite than the right, and the whole of this half of the face appeared flat; when the patient was requested to show her teeth, however, the lips moved equally on the two sides. The tongue was protruded straight and showed no tremor. The movements of the palate and larynx were normal.

The upper edge of the right optic disc was blurred and swollen; the swelling extended over the fundus on the inner side: the veins appeared normal. On the left side there was some œdema around the disc and indefinite patches of white exudate were seen on the inferior aspect of the fundus; the line of the inferior temporal artery around the disc on this side could not be traced: the other arteries were small, but on this side the veins were all slightly enlarged. The intra-ocular tension of both eyes was high. The patient

complained of severe pain in the back of the eye, made worse by light. Vision with each eye was fair and the visual fields to coarse testing not grossly impaired.

Hearing was normal, but the patient complained of a noise as of "water rushing through my head." The drums appeared healthy.

The lymphatic glands were not enlarged. A heaving impulse was felt in the fifth space in the mid-clavicular line. The second cardiac sound at the aortic area was accentuated, the first sound at all areas normal and there were no bruits. The lungs were unaffected and the chest moved normally. The wall of the radial artery could be felt, but was not abnormally thick. The blood-pressure was not greatly raised. The liver and spleen could not be felt and to percussion were not enlarged. The patient was constipated. The quantity of urine passed in twenty hours varied from 12 to 44 oz. The urine contained neither albumen nor sugar and casts were not present.

The rate of the pulse varied from 68 to 76 per minute, the rate of respiration from 20 to 24 per minute. The temperature throughout was raised; on admission it was 99.8° F., before death it attained the height of 103° F.

For eight days after admission the patient appeared to improve, her headache became less severe and her mental condition brighter. On December 22, a relapse set in; she became comatose, and passed urine and faeces incontinently into the bed, whilst the rate both of the pulse and of respiration rose. Venesection on the 24th led to no improvement in symptoms or general condition. Death occurred from respiratory failure on the morning of the 30th, seventeen days after admission and seven weeks after her first seizure.

An autopsy was performed on December 31 (P.M. 1181/1907). A ruptured aneurysm, of the size of a pea, was found at the junction of the left anterior cerebral and anterior communicating arteries. Around this aneurysm old and recent hæmorrhage into the meninges had occurred. The recent hæmorrhage had caused laceration of the brain substance and caused a rupture into the right lateral ventricle. A second, unruptured aneurysm of about the same size was found at the junction of the right carotid and right posterior communicating arteries. The brain weighed 1,474 grm. The left carotid artery at its point of bifurcation was slightly dilated. The heart generally, and more especially the left ventricle, was hypertrophied. Weight of heart 453 grm. As evidence of atheromatous changes a few minute fatty plaques were observed in the intima of the basilar and right posterior cerebral arteries; a few fatty plaques in the wide coronary arteries; fatty flecks and streaks in the carotids; three large fatty, slightly calcareous buttons and numerous fatty, slightly calcareous plateaux and flecks in the aorta and a fatty patch in the aortic cup of the mitral valve. The intima of the femoral arteries was hypertrophied and the media of these vessels showed evidence of slight degeneration. The kidneys were atrophic and together weighed 270 grs. The lungs showed atrophic emphysema with hypostatic congestion.

Under the microscope the wall of the aneurysm on the anterior cerebral artery was seen to consist of fibrous and a few small shreds of elastic tissue;

no muscle was seen. The anterior cerebral artery nearer its origin showed small thickenings of the intima composed of fibrous tissue and elastic fibres; the elastic fibres appeared to have been developed from the elastic stripe. In the site of the swelling at the bifurcation of the left carotid artery the media contained no elastic fibres; the swelling itself was formed partly of muscularis and partly of fibrous tissue.

There was a general hypertrophy of the intima of the aorta; this hypertrophy was found chiefly internal to the stripe and consisted of an inner dense fibrous and an outer fibro-elastic layer. At the site of the flecks the intima was further thickened and here formed nodules. The nodular thickening occurred internal to the elastic stripe. The external portion of this thickening was occupied by atheromatous debris, which was in part calcified. The layer of longitudinal muscles and elastic was not involved in the degeneration. The structure of the buttons was essentially similar. The media everywhere showed an excess of fibrous stroma. The intima of the femoral arteries was hypertrophied. A longitudinal layer of muscles was recognized between the elastic lamina and the stripe. Internal to the elastic stripe was a zone of concentric elastic fibres. The media contained many small spindle-form areas of degeneration.

A case of aneurysm of the right intracranial carotid artery close to the junction with the right middle cerebral, which led to death from cerebral hæmorrhage after giving rise for thirteen months to chronic headache. The first leakage apparently occurred whilst the patient was at stool and was accompanied by acute headache, vomiting, pains in the abdomen and legs. Ptosis of the right upper eyelid appeared fourteen days subsequently and on the sixteenth day a second leakage was ushered in by a convulsion and was followed by acute delirium. He was admitted to hospital on the twenty-first day and at that time showed complete paralysis of the right third cranial nerve with ptosis, optic neuritis, Babinski's sign on the left side, mental disorientation, free blood in the cerebrospinal fluid and albuminuria; under observation the reflexo-motor signs varied. Death occurred from respiratory failure on the thirty-sixth day after the onset of the acute manifestations.

Case 31.—30115/08, Charles E., aged 40, grocer, single, was admitted to the London Hospital under the care of Dr. W. J. Hadley on January 16, and died on February 1, 1908.

The patient was a slight, well-covered man of 40, with dark hair and grey beard, who looked somewhat older than his years. The history of his previous health is somewhat uncertain, as at the time of admission his mental condition was curious and he had no idea of either time or space.

He stated that his health had been uniformly good until the age of 38, two years before admission; he then suffered from an attack of "appendicitis," for which he was operated upon at St. Bartholomew's Hospital, E.C. After

this operation for eight months his health was fair. He then became subject to recurring attacks of occipital headache; the attacks were not severe enough to keep him from work. He denied all venereal infection and had not been addicted to alcoholic excess. For many years he had been deaf in his right ear in consequence of an attack of otitis media in childhood. He was an only child. There was no family history of vascular or nervous disease.

At 11.30 p.m. on December 27, 1907, whilst at stool, he was seized with severe abdominal pain, "shooting down my back and into my legs"; he passed a large stool and then "an electric shock seemed to run up my back into the top of my head." He managed to walk indoors but seemed "dizzy and queer." For half an hour he suffered from an intense headache and then vomited a large black vomit; the vomiting eased the pains in his head. He went to bed and immediately fell asleep. On the morning of the 28th he felt ill; a doctor was called in, who found some paresis of the patient's left leg. Between December 28 and January 16, when he was admitted, he complained of constant, severe pain in the lower part of his back, and of weakness of the legs. On January 10, ptosis of the right eye was noticed. On January 11, he suffered from a seizure which lasted for about fifty-five minutes; it came on suddenly, and in it he was "stertorous, cried out, and became stiff all over." The seizure itself was followed by shrieking and violent delirium, for which he was injected hypodermically with morphia. On the four succeeding nights he was delirious, and on the night of the 15th to 16th he had "five attacks with delirium and excitement."

On admission, twenty days after the onset of the illness, he made few complaints; he lay comfortably in bed and talked freely. He answered questions readily and volunteered sensible information. He had little idea of time or space; four hours after admission he stated that he had been in hospital three days: attempts to rectify this impression received the reply, "Well, I've been here three days, I know."

Speech was unaffected, and throughout his stay in hospital he did not vomit.

On the left forearm, just above the head of the radius, was a healing abrasion, brought about in his violent struggles when delirious, and over the sacrum were patches of reddened and roughened skin. The left knee was swollen, tender and slightly reddened, and the joint contained excess of fluid. The skin over the left heel was abraded. There was no anæmia and the lymphatic glands were not enlarged. On admission the temperature was 97° F., the rate of pulse 64 per minute, and the rate of respirations 30 per minute.

There was no absolute paralysis of any muscle, yet the patient was unable to turn himself in bed. All voluntary movements were carried out without precision in a clumsy, jerky fashion. The tone of the muscles of the extremities was normal and no abnormal muscular twitchings were observed. Spontaneous movements of any sort rarely occurred and under observation the left leg was never moved. He complained of no spontaneous pains and

to testing with cotton wool, the prick of a pin and for the recognition of passive movement no sensory loss was discovered.

Neither knee-jerks nor ankle-jerks could be elicited. On the right side the plantar response was flexor, on the left an extensor response was obtained. Kernig's sign was not present on the left, on the right it was doubtfully obtained.

The vessels of the optic fundi were full and some œdema was seen along their course; the edges of the discs were sharp and no hæmorrhages were observed. On the right side he could neither appreciate the ticking of a watch nor the sound of a tuning-fork applied to the mastoid; both drums appeared normal. Smell and taste were unaffected.

The right upper eyelid drooped and could not be raised voluntarily, the left lids moved normally. The right external rectus muscle acted well, but the remaining muscles moving the right eyeball were completely paralysed; on the left side all ocular movements were normal. Nystagmus was not present. The right pupil was widely dilated and did not react to light or on attempted movements of this eye; the left pupil was moderate in size and reacted normally to light and on accommodation. The facial movements were normal. The tongue was protruded straight and held steadily. The movements of the palate and larynx were unaffected.

On admission the actions of the bladder and rectum were controlled and the movements of the spine were unaffected.

The apex-beat of the heart was felt in the fifth space just internal to the mid-clavicular line; the cardiac sounds were clear. There was no abnormal dulness over the lungs, and the breath sounds were normal.

A well-healed scar, 4 in. long, was seen over the right iliac fossa. The liver and spleen could not be felt, and to percussion there was no evidence of any enlargement of these organs.

The quantity of urine passed in twenty-four hours varied from 24 to 64 oz., and the specific gravity from 1021 to 1028. The urine was acid, and, on boiling, yielded a thick cloud of albumin; blood and sugar were never found. On standing, a quantity of floating mucus was deposited; this deposit consisted in the main of broken-down pus cells and squamous epithelial cells, but in it occasional hyaline casts were seen.

On January 18 lumbar puncture was performed. Cerebrospinal fluid escaped under considerable pressure. This fluid was bright red in colour and uniformly stained with blood. On microscopic examination many red cells and a few polymorphonuclear leucocytes only were found; bacteriologically the fluid was sterile.

For a few days after admission the patient's general condition improved. The headache became less severe, and his mental condition clearer; he now complained of a sensation "as if I were falling backwards." On the nights of the 17th, 18th, and 19th he was delirious; he called to imaginary persons, and received imaginary answers, but in the daytime he was more or less rational in his behaviour, though in general he lay with his eyes closed, complaining

of little and speaking only when addressed. He was now able to carry out certain voluntary movements, but when left to himself performed few.

The physical signs of disease varied from day to day and from hour to hour. Sometimes on the right side a knee-jerk could be obtained, at others it was absent; at still others it was grossly exaggerated; the left knee-jerk also varied, and occasionally was absent. The plantar responses also showed variations; sometimes the right would be extensor, at others flexor; the response on the left side varied similarly, but not synchronously. The mental state gradually improved between January 19 and January 30; spontaneity returned, headache was no longer complained of, the sensation of falling backwards disappeared, and the nocturnal delirium ceased.

In the early hours of January 30 the patient was seized with severe headache; the headache was at first chiefly frontal, but soon spread backwards over the occiput and into the neck. It was accompanied by pressure tenderness of the scalp. There was, however, no rigidity of the muscles of the neck or of the back. The onset of the headache was not accompanied by any corresponding alteration in the rate of the pulse or of respiration.

At midday, on the 30th, he suddenly became worse and lost consciousness; breathing became shallow, and occasionally stertorous. The right pupil remained dilated, but the left contracted to the size of a pinhead. The rate of the pulse remained about 100 per minute.

Lumbar puncture was now performed, and cerebrospinal fluid under considerable pressure escaped in a steady stream. The fluid was fairly clear, and intimately mixed with bright red blood; two ounces were collected. The breathing became deeper and more regular, and a movement of the right hand to the head, apparently of a voluntary nature, was observed. Consciousness of his surroundings, however, did not return. Frequently repeated flexion-extension movements of the right thigh were now noted.

At 9.30 p.m. on this day he lay flaccid and unconscious. The left pupil was small, the right dilated, but not to such a great extent as heretofore. There was definite unsteadiness of the eyes on looking outwards of a nystagmoid nature. The right eye showed much greater freedom of movement than had been previously observed. Exposure of the eyes to light irritated the patient, and was followed by movements of the head and general restlessness of the body. At this time breathing was regular, and expiration was accompanied by a flapping of the cheeks and a short groan. Flexion of the right thigh was frequently seen: all the other extremities lay flaccid by the trunk. The knee-jerks could not be elicited. On the right side there was a ready extensor plantar response; on the left no plantar response could be obtained. The wrist- and elbow-jerks were absent. On the right side Kernig's sign was positive, on the left negative. No reaction to painful pressure or to the prick of a pin could be obtained from any portion of the head, trunk, or extremities. The right half of the face in both its upper and lower portions was completely paralysed, and the ptosis of the right upper lid persisted.

Eight hours later the patient's condition again became worse. Lumbar puncture was again performed, and eleven drachms of bright red fluid were obtained. After this he became steadily weaker, the breathing took on the Cheyne-Stokes' characters, and the respiratory passages filled with mucus.

Death from respiratory failure occurred twenty-four hours later at 8.30 a.m. on February 1, 1908, thirty-six days after the initial seizure.

At the autopsy performed on the afternoon of the day of death only an examination of the head was permitted. A small ruptured aneurysm, of the size of a haricot bean, was found on the right intracranial carotid artery close to the origin of the middle cerebral artery. The right temporal convolution as far as the second temporal sulcus was almost completely destroyed. Over the base of the brain and over the vertex and the region of the Sylvian fissure on the right side there was considerable subarachnoid and subpial hæmorrhage, and around the aneurysm there was a considerable quantity of older blood-clot. The lateral and fourth ventricles were distended with blood-stained fluid. Otherwise the cerebral arteries appeared quite healthy, and showed no sign of inflammation or atheromatous change.

A case in which the autopsy revealed a ruptured and partially thrombosed aneurysm of the left middle cerebral artery near the base of the brain, considerable atheroma of the cerebral arteries, severe general arterial degeneration, and slight cardiovascular hypertrophy, in a woman aged 67. Eighteen years before death this patient, after complaining of left-sided local headache, had suffered a right hemiplegia with motor aphasia from which she almost entirely recovered. Seven months before death she developed ptosis and supraorbital neuralgia on the left side, the pains of which for five months were relieved by an injection of alcohol. Eighteen days before death a sudden apoplectiform seizure occurred with development of motor aphasia, œdema of the soft tissues around the left eye, complete paralysis of the left third cranial nerve and ptosis and noises in the ears; partial recovery. Seven days before death, after a seizure, paralysis of the right face, tongue, and arm, and severe hebetude appeared. Final seizure and respiratory failure on day of death.

Case 14.—40432/1913. Jane P., aged 67, married, was admitted to the London Hospital under the care of Dr. W. J. Hadley on February 11, and died on February 23, 1913. In 1891, at the age of 45, after suffering for several years with chronic left-sided headache, she had a seizure which was followed by a right-sided "hemiplegia and motor aphasia"; at this time she was "unable to talk" for fourteen days, and in bed for six weeks. The right hemiparesis completely disappeared, and except that she was still subject to recurrent episodic attacks of severe pains in the head, for the next twenty years her health was good. In February, 1912, she suffered an attack of erysipelas. In June, 1912, she was in-patient at the Croydon Hospital, complaining of trouble in opening her left eye and intense supraorbital

neuralgia. For the neuralgia, alcohol was injected into the left supraorbital nerve. After the injection she was never able to raise her left upper eyelid, but the pain was relieved. About Christmas, 1912, the left supraorbital pains returned, and on December 31, 1912, the supraorbital nerve was again injected with alcohol; this injection, however, yielded no relief. On February 3, 1913, she suffered from a seizure in which consciousness was lost; on the return of consciousness she was unable to talk; she knew what she wanted to say, could write and draw, but could not utter the words. On February 4, 1913, speech returned. She then became subject to nocturnal delirium, and her ideation became inconsequent. After the seizure until admission she was kept in bed.

On admission: The tissues around the left orbit and in the left temporal region were oedematous and pitted slightly on pressure. Cerebration was slow and ideation defective. In general she lay in bed in a dazed and drowsy condition taking little interest in her surroundings. At night she was restless, noisy, and made attempts to get out of bed. To questioning she answered rationally and quickly. Speech was not affected. She was well orientated and delusions were not present. Memory was defective.

She was completely unable to open the left eye and the left upper lid drooped. The external rectus and superior oblique muscles acted normally, but the power of movement by all the muscles supplied by the left third cranial nerve was extremely feeble. The left pupil was dilated and did not react either to light or attempted convergence; the right pupil was of moderate size and reacted normally. The movements of the jaws, face, palate, tongue, and larynx were unaffected. There was considerable sensory loss over the area of skin supplied by the left supraorbital nerve, probably consequent on the injection given on December 31, 1912; hyperalgesia and loss of sensation were not discovered elsewhere in the skin supplied by the fifth cranial nerve. Hearing was unaffected, but the patient complained of a "roaring noise in both ears": the drums appeared healthy. The optic discs and ocular fundi on both sides appeared healthy. Smell and taste were unaffected.

There was no motor paresis of the limbs or trunk, and the tone of the muscles of the limbs was normal. No sensory disturbance over the body or extremities was discovered.

The knee-jerks and ankle-jerks were not exaggerated, and both plantar reflexes gave a flexor response. Neither upper nor lower abdominal reflexes could be obtained. The wrist- and elbow-jerks were normal and a jaw-jerk could be obtained.

The action of the sphincters was controlled.

The chest was emphysematous and the area of cardiac dullness small. A feeble cardiac impulse could be felt in the fifth space just inside the mid-clavicular line. The cardiac sounds were normal. The wall of the radial pulse could just be felt but the blood-pressure was not unduly high. No abnormal signs were discovered in the abdomen. The urine contained a cloud of albumin, but no sugar; its specific gravity varied from 1017 to 1025. The patient had suffered from recurrent attacks of epistaxis, but no abnormal

appearances were detected in the nose, and all the sinuses on illumination appeared normal.

On the second evening after admission she was noisy, made irrelevant remarks and suffered from hallucinations and illusions. About 10.30 p.m. on this day she suddenly fell back in bed; her breathing became stertorous and dyspnoëic; she lost consciousness, and for two or three minutes moved her limbs violently. After the seizure she was very irritable and restless, and yet could not move her limbs voluntarily. The puffiness around the left orbit increased. On examination complete paralysis of the left third cranial nerve, weakness of the lower half of the right face and of the right half of the tongue, and a monoplegia of the right upper extremity with increased reflexes were discovered. The right knee-jerk was more brisk than the left, but ankle-clonus was not present and both plantar reflexes gave a flexor response. On the morning of the 13th speech was impaired, but the lower extremities and left arm were under voluntary control; and the patient suffered from retention of urine with overflow. She could understand written and printed words, and attempted to answer the questions. During the whole of the 14th, respirations were of the Cheyne-Stokes type. On the 15th she talked freely but her remarks were inconsequent and nonsensical. From this time until the 21st her condition altered little; on this day she again suddenly lost consciousness and died from respiratory failure.

At the autopsy, P.M. 140/1913, performed on February 24, a ruptured and partially thrombosed aneurysm, 3 cm. in diameter, was found on the left middle cerebral artery near the base of the brain. No atheromatous changes were seen in the aneurysm itself, but the cerebral arteries generally were wide and showed severe atheromatous changes. The left third cranial nerve was small and grey in colour. The meninges in the neighbourhood of the aneurysm and in the right Sylvian fissure were deeply stained with altered blood-pigment and much matted. The myocardium everywhere was fatty. The wall of the left ventricle was 2 cm. in thickness. The base of the mitral and aortic cusps was slightly thickened. Fatty plaques and flecks were observed throughout the thick-walled aorta and calcareous plaques were seen in the aortic arch and abdominal aorta. The coronaries were wide and showed many thick-set fatty streaks and plaques, whilst the carotids were studded with fatty streaks. In the posterior parts of both lungs evidence of purulent bronchitis and hypostatic broncho-pneumonia was discovered. The kidneys were "granular;" in colour they were red, and their surfaces were irregular and showed subcapsular nodules. The cortex was narrowed, and owing to the presence of large arcuate arteries showed a tortuous pattern.

In *nine* other cases multiple seizures from partial ruptures of a cerebral aneurysm occurred.

Case 23 (p. 284) was that of a grocer, aged 41, who had been under more or less continuous observation at hospital over a period of sixteen years, and had complained of recurring attacks of headache, and been

blind of an anæsthetic left eyeball for three years. The *post-mortem* examination showed that he died from the rupture of an aneurysm of the size of a currant-grape at the junction of the right anterior cerebral and anterior communicating arteries. In this patient the first bleeding occurred forty-three days, a second twenty-five days, a third seven days, and a fourth twenty-four hours before death in coma.

Case 22 (p. 287) was an example of multiple leakages and seizures due to the rupture of a small aneurysm of the left posterior cerebellar branch of the basilar artery. At the autopsy a mass of blood-clot which had pressed upon the pons, cerebellum, medulla, and the occipital lobe of the left cerebral hemisphere was discovered. The patient was a married woman, aged 42, who, when aged 25, and 8 months pregnant of her second child, had suffered a transient hemiplegia affecting the right face, tongue, arm, and leg, and who for the five months preceding death had complained of slight epileptiform (*petit mal*) attacks with visual auræ. The first evidence of definite leakage was a seizure nineteen days before death, followed by a second twelve days and a third ten days before the fatal issue. On admission to hospital the patient was delirious, and showed paresis of the left half of the face, right hemiplegia, affecting the arm and leg, and complained of tenderness in the left occipital region and stiffness of the neck; the head was held in the left cerebellar attitude, but no nystagmus was observed; in the right eye early optic neuritic changes were present.

Case 16 (p. 289) at autopsy showed a ruptured aneurysm, of the size of a pea, at the junction of the left anterior cerebral and anterior communicating arteries. The patient, a carpenter, aged 53, sustained a first seizure whilst watching a football match twenty-seven days before death. This seizure was followed by a state of delirium and a complaint of headache and cerebral vomiting; later he began to suffer from epileptiform attacks, and became clumsy in all his movements. Five days and three days respectively before death he sustained a second and a third seizure; after the third seizure he was admitted to hospital, where he died.

In Case 29 (p. 292) the rupture of an aneurysm, of the size of a pea, on the left anterior cerebellar artery caused the death of a young man, aged 22. Six days before death he sustained his first seizure, followed by a state of mental instability. Three days later a second seizure led to drowsiness, left facial paralysis, bilateral corticospinal interference, left cerebellar posture of the head, stiffness of the neck, and the appearance of free blood in the cerebrospinal fluid, and to death without any recovery of consciousness.

Case 3 was that of an upholsterer, aged 60, who died from the rupture of an aneurysm of the size of a pea on a central branch of the right middle cerebral artery. At the autopsy this patient also showed a smaller, unruptured aneurysm on a second branch of the same vessel, severe atheroma of all the cerebral arteries, severe general arterial degeneration, and great cardiovascular hypertrophy. Two years before death this patient had suffered a monoplegia of the left lower extremity, from which he soon entirely recovered; fifty hours before death a second seizure led to paresis of the left arm, abolition of the right corneal reflex, and a state of deep coma, from which he never recovered. After admission to hospital he suddenly became convulsed; after the convulsion the left-sided paresis had increased, and signs of left cortico-spinal interference appeared.

Case 12 was that of a woman, aged 46, who was admitted to hospital in an irritable condition after a seizure, which had come whilst she was minding her fruit stall in the street, complaining of some subjective weakness of the left upper extremity, right-sided headache, leading to nausea and vomiting, and giddiness, but showing no optic neuritis or other sign of intracranial affection. Three days after admission all her symptoms had cleared, and on the fourth day she discharged herself, to be readmitted on the fifteenth day after the initial seizure in a deeply unconscious state, which was again said to have come on suddenly, and from which she never recovered.

At the autopsy a ruptured aneurysm was found on the rightmost of three anterior cerebral arteries just beyond the origin of the anterior communicating, of the size of a pea. The convexity of the right cerebral hemisphere was covered with old hæmorrhagic clot, and in the arteries generally there was a moderate grade of degeneration and a moderate degree of cardiovascular hypertrophy.

Case 15 was that of a married woman, aged 60, who six months before death suffered from an attack of "inflammation of the lungs," after which she never recovered her health, but became subject to recurring attacks of severe headache. The initial seizure in this case occurred whilst the patient was in bed on the seventy-fourth night before death; she woke with a sudden severe headache, leading to vomiting. This attack of headache only lasted one day, but twenty-six days later she became "dazed" after a "bad shivering attack," and in this condition was admitted to hospital. This patient showed numerous scars on the shins, apparently due to old varicose ulcers, for her serum reacted negatively to the Wassermann test. The blood-pressure in the

arm measured 188 mm., and the urine contained a trace of albumen. She complained of severe frontal headache, but the fundi appeared healthy. The left face showed a slight upper motor neuron weakness, otherwise no affection of the cranial nerves was detected. Motion, sensation, the reflexes, and the action of the sphincters were unaffected. Despite the negative Wassermann reaction the condition of this patient was thought to have a syphilitic basis, and she received an injection of 0.6 grm. neosalvarsan. After this injection the headache became more severe and more persistent, and she began to vomit several times daily. Twelve days after the injection insomnia, nocturnal delirium, "mental" incontinence of urine and faeces, and delusions, made their appearance, and the paresis of the left face became more noteworthy, whilst the quantity of albumin in the urine increased. These manifestations altered little until the day of death. On that day, whilst sitting in a chair in the ward, she suddenly fell backwards, and a few minutes later died from respiratory failure. At the autopsy all the large basal cerebral vessels were dilated, and on the right middle cerebral artery was an aneurysm of the size of a cherry-stone, which had ruptured. In the great vessels was evidence of severe arterial degeneration, and in the cardiovascular system generally some slight hypertrophy.

Two years before death a packing-case maker, aged 36 (Case 25), who for many years had been addicted to alcoholic excesses, suffered a "fainting attack, after which he was never the same man." At the time of the attack, and for three weeks afterwards, he complained of an unbearable pain in the head, which gradually became less severe, but never entirely ceased. Twelve hours and a half before death this patient was at work, when he suddenly shouted that the headache had returned, and that he felt as if the top of his head would burst; then he became giddy, seemed to lose himself, and for the next hour and a half struggled and threw himself about. On admission he was deeply comatose and stertorous. At the autopsy an aneurysm of the size of a cherry-stone, which had ruptured, was found on the left intracranial carotid artery. In the heart and vessels few signs of disease were present, but the wall of the aneurysm itself showed atheromatous changes.

The last of this class is Case 26, that of a married woman, aged 36, who during the two preceding winters had suffered from chronic bronchitis. Three months before death she began to complain of episodic attacks of severe left frontal headache. Three days before death she was out shopping when she suddenly "came over giddy,"

complained of severe left temporal headache, fell in the street and was taken home and put to bed. Throughout the next three days the headache persisted, and she remained in bed at home. On the night of her death she was found deeply unconscious, having vomited, showing proptosis of the left eye and widely dilated fixed pupils, whilst the knee-jerks were abolished and both plantar responses were extensor. At the autopsy three aneurysms were found on the cerebral vessels, a ruptured aneurysm of the size of a grape-stone at the junction of the left intracranial carotid and posterior communicating arteries and two unruptured aneurysms on the right middle cerebral artery. The more proximal was the smaller and lay in the fork of a primary division of the middle cerebral, whilst the more distal, a little larger than a grape-stone, lay slightly nearer the base of the brain. Atheromatous changes were present in the peripheral portions of the unruptured aneurysms, but otherwise the cerebral arteries appeared normal, and there was only slight general arterial degeneration and no cardio-vascular hypertrophy.

IN THIRTEEN CASES MULTIPLE SEIZURES OCCURRED AT VARYING INTERVALS
BEFORE DEATH.

Case	Sex	Age	First seizure	Second seizure	Third seizure	Fourth seizure	Fifth
26	♀	36	3 days	8 hours	—	—	—
29	♂	22	6 „	2 days	—	—	—
12	♀	46	19 „	16 hours	—	—	—
30	♂	19	24 „	3 days	2 days	—	—
23	♂	41	25 „	7 „	Few hours	—	—
16	♂	53	27 „	5 „	3 days	2 days	Few minutes.
31	♂	40	36 „	21 „	8 hours	—	—
4	♀	49	50 „	33 „	8 days	—	—
15	♀	60	74 „	48 „	Few minutes	—	—
25	♂	36	2 years	12 hours	—	—	—
3	♀	60	2 „	50 „	—	—	—
22	♀	42	17 „	6 months	5 days	—	—
14	♀	67	22 „	8 „	18 „	1 hour	—

Patients in whom abnormal conditions of the vessels are suspected are always warned against the effects of a sudden rise in blood-pressure associated with violent voluntary efforts and acute emotional experience. In this series of cases the importance of this warning is well illustrated. The manifestations of the initial rupture in Case 28, that of a young man aged 22, occurred whilst the patient was competing in a public cycle race, and in Case 16, that of a carpenter aged 53, while the patient was watching a local football match and overflowing with excitement. Case 31 sustained his first seizure whilst straining at stool; Case 5 whilst at work painting; Case 29 when at work in the stable; Case 25 when lifting a heavy packing-case; and Case 30 whilst reaching

upwards to paint the top of a window. Seven examples of rupture whilst in the street occurred: Cases 1, 2, 9, 10, 12 (when minding a street-stall), Cases 24 and 26 (shopping); and in one case (Case 27) the acute manifestations developed whilst the patient was in the bathroom, and in another (Case 17) during a bout of coughing.

Although aneurysm is one of the relatively common forms of "intracranial neoplasm," when the tumour is due to changes in the media of the arterial wall it grows slowly and only rarely does it attain any considerable size, hence before rupture signs of increased intracranial pressure—hebetude, headache, vomiting, and optic neuritis—are also rare. In this series of cases *in no single instance* where at autopsy the aneurysm was found to be associated with changes in the media only was there clinical evidence that the aneurysm before rupture had led to the development of *optic neuritis*. In Case 25 the patient long before the final rupture took place was blind of his left eye, but here the whole eyeball, which was anæsthetic, shrivelled. On the other hand, amongst 555 cases collected by Beadles, in 16·4 per cent. signs of "tumour only" were present, and in a further 20·7 per cent. "signs more or less suggestive of tumour" occurred before rupture. Aneurysms of embolic origin without an attendant diffuse septic meningitis have only on extremely rare occasions given rise to signs of "increased intracranial pressure," and in this series optic neuritis in association with embolic aneurysm was not noted, although in Case 9 the left disc appeared slightly swollen and the whole of the fundus on this side had a glassy appearance. Cerebral aneurysms of syphilitic origin are more frequently associated with fundal changes, but in this class of case a reactive meningitis is practically always present, and the evaluation of the relative importance of the meningitis and the aneurysmal formation as the cause of these changes is, and has been, always difficult.

In this series of cases of aneurysms due to changes in the media after rupture had occurred the condition of the optic fundi was noted in 16 cases; in 10 the discs, vessels, and fundi were pronounced healthy, and in 6 abnormalities were described.

In Case 4 (p. 252) the ruptured aneurysm was found at the junction of the left anterior cerebral and anterior communicating arteries. Here the upper edge of the right optic disc was blurred and swollen and this swelling extended over the inner side of the fundus; the arteries and veins appeared normal. On the left side there was some œdema around the disc and indefinite patches of white exudate were seen on the

inferior aspect of the fundus, whilst the line of the inferior temporal artery near the disc could not be traced; the other arteries were small, but on this side the veins were all slightly enlarged.

In Case 16 (p. 289) the aneurysm was found at the junction of the left anterior cerebral and anterior communicating arteries; here the right optic disc and fundus appeared pale and the edges of the disc clearly defined, but whilst the arteries were small the veins were engorged. On the left side the disc was swollen ($1\frac{1}{2}$ D.) and its edges blurred and the veins were more engorged than on the right.

In Case 22 (p. 287) the ruptured aneurysm was found on the left posterior cerebellar branch of the basilar artery, and the patient suffered amongst other complaints from epileptiform attacks with visual auræ. In this case the left fundus was described as of healthy appearance, whilst on the right the veins were engorged, the disc pink in colour, its edges indistinct and blurred, whilst the arteries were unaffected.

In Case 27 an aneurysm on the left intracranial carotid artery, of the size of a pea, had ruptured; just before death the right optic disc was described as healthy but the left was said to be swollen.

In Case 30 (p. 249) an aneurysm measuring 1.5 cm. by 1 cm. was found at the junction of the left internal carotid and posterior communicating arteries. The right optic fundus of this patient sixteen days before death showed engorgement of the veins and some œdema of the lower quadrants, whilst on the left side no changes were detected. On the day of death the veins of the right fundus were full and the edges of the inferior and temporal quadrant of the disc blurred, whilst on the left side the whole fundus appeared hazy and the disc showed definite swelling of about $1\frac{3}{4}$ D.

In Case 31 (p. 256), a ruptured aneurysm of the right intracranial carotid artery close to the origin of the middle cerebral artery of the size of a haricot bean was found; twenty days after the initial seizure the veins of both optic fundi were large, and along their course some œdema was present, but the edges of the disc were unaffected.

Headache.—The headaches associated with the presence and rupture of intracranial aneurysms do not differ from those associated with pathological intracranial conditions owing to other causes, and frequently give rise to nausea and vomiting. In general, when a patient complains of localized pain in the head, and a cerebral aneurysm is suspected on other grounds, the aneurysm will be found on the same side of the circle of Willis as the headache (Cases 12, 16, 22, 26, 27 and 30), and if the headache is worse in the frontal or orbital region it is likely that

the affected vessel lies in front of the point of entry of the carotid artery into the cranial cavity (Cases 4, 15, 16, 20, 25 and 26), whilst, on the other hand, the complaint of pain localized to the occipital and upper cervical region renders the affection of a vessel in the posterior cranial fossa probable (Cases 22, 30 and 31).

In six of the 31 cases (19·3 per cent.), episodic attacks of headache were the first clinical manifestations which could be attributed to the development of a cerebral aneurysm; in all these cases at a later date the sac of the aneurysm leaked and before death signs of meningeal hæmorrhage appeared. Case 4, a woman, aged 49, for two years before death was subject to attacks of frontal headache and complained of insomnia and noises in the head. Case 27, a compositor, aged 28, for nineteen months before he came under observation suffered from severe attacks of left-sided headache, and for six months from attacks of giddiness complicating the headache. Case 31, a grocer, aged 40, complained of chronic occipital headache for thirteen months before the final ruptures; whilst Case 15, a married woman, aged 60, during the nine months before death suffered from recurring attacks of headache and during her last ten weeks showed defective cerebration. Case 26, a woman, aged 36, for three months before the final seizure complained of frontal and temporal headache limited to the left half of her head; and finally, Case 18, eight days before admission developed acute headache and nausea; she vomited several times, but not until six days later did any local signs of intracranial interference appear.

The interferences with *general cerebral functions* associated with the presence of an unruptured or of a ruptured cerebral aneurysm are not characteristic. Before rupture the blood-supply of some small portion of either hemisphere may be defective and thus produce symptoms, but this appears to be exceptional. After a partial leakage the affected vessel may become thrombosed and localized cerebral softening may thus be set up, or local destruction and ploughing up of portions of the hemispheres may be caused by the blood which has leaked primarily into the meninges. Sudden hæmorrhages are manifested by apoplectic attacks and the development of a more or less deep state of coma, and if the hæmorrhage be large, death without recovery of consciousness occurs. Smaller leakages give rise to less complete abolition of function, and thus states of hebetude, apathy, drowsiness, inattentiveness, associated with irritability, "strangeness in behaviour," "hysterical attacks," defective ideation, delirium, insomnia, nocturnal psychoses and the like may arise, and, if the surface of the cerebrum

be affected and yet not destroyed, convulsions of all sorts may appear.

Hemiplegia.—The motor affections associated with ruptures of cerebral aneurysms depend upon the site of the lesion affecting the corticospinal connections, and this may be cortical, basal, or pontine. Cortical affections produce more limited manifestations than do affections at other points on the course of the pyramidal tracts. In Cases 3, 7, 15, due to an aneurysm on the middle cerebral artery, an affection of the pyramidal tract in the cortex or subcortex was noted, and in Cases 16 and 22 convulsions of an epileptiform type were associated clinically with the finding of localized damage to the cortex of the cerebral hemispheres. In Cases 3, 14 and 30 the Weber syndrome (paralysis of one third cranial nerve with crossed affection of face and limbs) was present, and in Cases 22 and 29 the pontine type of hemiplegia with facial paralysis and crossed paralysis of the limbs occurred, whilst in Cases 6, 17 and 26 pressure due to the rupture of aneurysm at the base of the brain led to bilateral interferences with the upper motor neuron connections.

At the base of the brain the cerebral arteries bear close relation to the *cranial nerves*. One would expect, therefore, that when an aneurysm had developed upon one of the basal vessels pressure effects upon one or more cranial nerves would not infrequently occur and might prove of localizing value in diagnosis. Judged by this series of cases, however, cranial nerve affection rarely occurs until the wall of the aneurysm ruptures. In Case 14 (p. 260) alone did both the clinical history and the autopsy reveal changes of old standing in any cranial nerve; in this case the third nerve on the left side was found grey, thin and stretched over the sac of an aneurysm, 3 cm. in diameter, on the left middle cerebral artery; the aneurysm had also pressed upon the left Gasserian ganglion and caused a supra-orbital neuralgia on that side.

In *no case* was any definite evidence, clinical or pathological, of an affection of the olfactory nerves obtained.

In Case 23 (p. 284) in association with an aneurysm at the junction of the right anterior cerebral and anterior communicating arteries was a shrivelled and anæsthetic left eyeball and atrophic, grey, left optic nerve. In no case in this series was there any evidence of hemianopsia or other affection of the optic tracts, but in two cases the one recorded by Byrom Bramwell [7] and the other by Weir Mitchell [26] bitemporal hemianopsia due to the presence of a large saccular aneurysm in the infundibular region occurred.

In cases of cerebral aneurysm after rupture the third pair of cranial nerves are those most commonly involved. Ptosis, an affection of the pupils and even total paralysis of the third cranial nerve on one side, are not infrequent.

On the admission of Case 31 (p. 256) to hospital, the right upper eyelid was dropped and could not be raised, the right pupil was widely dilated and fixed, and all the muscles moving the eyeball supplied by the right third cranial nerve were completely paralysed. At the autopsy a ruptured aneurysm on the right intracranial carotid close to the origin of the right middle cerebral artery was found. Case 30 (p. 249), after a seizure, showed a similarly complete paralysis of all the muscles supplied by the left third cranial nerve; at the *post-mortem* examination this nerve was found to be stretched over and adherent to the posterior extremity of a ruptured aneurysm on the posterior communicating artery close to the bifurcation of the intracranial carotid. The patient in Case 27 was deeply comatose when admitted; in him the right pupil was small, the left widely dilated, and neither pupil reacted to the light. Here the ruptured aneurysm was found on the left intracranial carotid. In Case 26, proptosis of the left eyeball, together with fixity of the pupils, was observed; a mass of blood-clot was found at the autopsy pressing upon the left cavernous sinus; this had escaped from an aneurysm at the point of junction of the left intracranial carotid and posterior communicating arteries. Case 24 was moribund on admission; here the pupils were fixed and dilated and a rupture was found to have occurred from the right posterior communicating artery at its point of junction with the posterior cerebral. Case 23 (p. 284) after the second leakage showed severe ptosis of the right eye in addition to the atrophic left eyeball.

In Case 22 (p. 287), on admission to hospital, the left pupil was larger than the right, but both reacted normally to light; a left facial weakness and right hemiplegia affecting the arm and leg were also present in consequence of the leakage of an aneurysm on the left posterior cerebellar branch of the basilar artery. Cases 10 and 13 were deeply comatose on admission. In Case 13 neither pupil reacted to light and the size of both varied greatly from moment to moment; signs of bilateral corticospinal interference were present and at autopsy a ruptured aneurysm on the left anterior cerebral at its junction with the anterior communicating artery was found; whilst in Case 10 both pupils were immobile, and the right dilated and much larger than the left in a man, aged 55, who was admitted one hour before death; here the

aneurysm which had ruptured was found on the corresponding junctional point of the anterior cerebral and anterior communicating on the right side. Case 4 (p. 252) complained of diplopia, but showed no gross abnormality of the pupillary reactions; here complete ptosis of the left upper eyelid and paralysis of the right external rectus muscles were found consequent on the rupture of an aneurysm at the point of junction of the left anterior cerebral and anterior communicating arteries and the presence of a second unruptured aneurysm at the junction of the right carotid and posterior communicating arteries.

In two cases abolition of the conjunctival and corneal reflexes was of some localizing value. In Case 3 on the right side neither of these reflexes could be elicited, and with this loss was associated a paresis of the left upper extremity owing to the rupture of an aneurysm on the right middle cerebral artery; and in Case 25 the left corneal and conjunctival reflexes were completely abolished and the right considerably diminished in consequence of the rupture of an aneurysm on the left intracranial carotid artery.

Case 14 (p. 260) during the seven months preceding death suffered from a left-sided supra-orbital neuralgia and ptosis; alcoholic injections, which were given into the nerve, relieved the acute pains for a time but the patient soon relapsed. At autopsy a firm mass of blood-clot, which had escaped from the left middle cerebral artery, was found filling the cavernous sinus and pressing upon the Gasserian ganglion. The association of major trigeminal neuralgia with the presence of a cerebral aneurysm cannot be very infrequent, for in two other instances which have come under my notice since this series was closed I have seen autopsies which revealed a similar pathological condition, in one of which before death herpes ophthalmicus developed owing to the involvement of the Gasserian ganglion in the mass of blood-clot.

Facial paralysis, due to an affection of the nerve in its intracranial course, and after its exit from the pons, usually signifies that one of the cerebellar arteries is the source of trouble. In Case 29 (p. 292), at the time of admission a stable-boy, aged 22, showed a complete, peripheral type of left facial paralysis and right hemiplegia; at autopsy a ruptured aneurysm was found on the left anterior inferior cerebellar artery. In Case 22 (p. 287) the lower half of the left face was completely paralysed and the upper half weak, whilst the right arm and leg were spastic and parètic in association with a ruptured aneurysm on the left posterior cerebellar branch of the basilar artery.

Facial paralysis of cerebral origin associated with a more or less

complete hemiplegia may also occur in cases of ruptured cerebral aneurysm. Case 4, on admission, in addition to the paralysis of the left external rectus muscle and ptosis of the right eye, showed slight left facial paresis of cerebral origin; at autopsy two aneurysms were found, a ruptured one at the junction of the left anterior cerebral and anterior communicating arteries and an unruptured one at the junction of the right carotid and posterior communicating arteries. In Case 5 a right hemiplegia of arm and leg and some affection of the left extremities, together with a right facial paresis of upper motor neuron type, appeared in consequence of the rupture of an aneurysm at the point of junction of the left anterior cerebral and anterior communicating arteries.

In Case 7 an old man, aged 86, was admitted to hospital complaining of some difficulty with speech, and showing slight left facial weakness; four weeks later he died, and at the autopsy an unruptured aneurysm on the right middle cerebral artery near the base of the brain was found, and all the cerebral arteries were dilated and atheromatous. Case 15, a woman, aged 60, on admission complained of headache, giddiness, and cerebral vomiting, but the only definite sign of intracranial affection was a slight paresis of the left face, apparently of cerebral origin; at the autopsy, seven weeks later, an aneurysm which had burst was found on the right middle cerebral artery near the base of the brain. Case 30 (p. 249), at autopsy showed an unruptured aneurysm on the left posterior communicating artery; on admission to hospital this patient exhibited a complete paralysis of the left third cranial nerve and grave paresis of the right half of the face.

Deafness, as the consequence of an unruptured cerebral aneurysm, is not common. Case 20, a man aged 47, died in hospital of acute diffuse myelitis. Some months before death this patient suffered an "influenzal attack," which left him subject to severe frontal headache, and deaf of his right ear. At the autopsy an unruptured aneurysm of the size of a pea was found at the point of bifurcation of the right intracranial carotid artery.

Case 31, on admission, in addition to a complete paralysis of the right third cranial nerve, showed an almost total nerve-deafness of the right ear; the aneurysm which had ruptured was found on the right intracranial carotid close to the origin of the right middle cerebral artery.

Case 4 was the only example in this series of a patient who complained of "noises in the head and ears"; here a ruptured aneurysm was found on the left anterior cerebral artery at its junction with the

anterior communicating and a smaller unruptured aneurysm at the junction of the right carotid and posterior communicating arteries. In the literature of these cases buzzing noises in the head, hissing noises in the ears, waterfall noises, and even murmurs audible to the doctor, have been described.

In no single case in this series was any affection of the ninth, tenth, eleventh, or twelfth nerves below their nuclear origin discovered; and in no case did polyuria or glycosuria occur.

Pyrexia.—After a seizure consequent upon the rupture of the sac of a cerebral aneurysm of non-embolic origin, some degree of pyrexial disturbance is almost the rule, but in general the temperature reached is not high.

In Case 22 (p. 287) a rupture of an aneurysm on the posterior cerebellar branch of the basilar artery led before death to the development of a temperature of 105° F.; and in Case 18 the rupture of a similar aneurysm on the left anterior communicating artery to a temperature of 106° F.; but in no other case in this series did the thermometer record more than 103° F. In *five* cases (5, 6, 12, 13, and 29) the highest record was between 102° and 103° F.; in *two* cases (16 and 23) the highest point reached was 101° F., and in *six* cases (4, 14, 25, 27, 30, and 31) no temperature higher than 100° F. was observed, and in *ten* cases (2, 3, 9, 10, 15, 17, 21, 24, 26, 28) no record showing a higher figure than 99° F.

Stiffness of the neck, after the rupture of a basal cerebral vessel, is a not uncommon manifestation and source of complaint. The appearance of this symptom implies that blood has leaked into the posterior cranial fossa, and that clot has surrounded and compressed the lower medullary and upper cervical nerves. The presence of this symptom, therefore, renders probable the finding of the aneurysmal sac either on the basilar artery (or one of its branches) or on the posterior communicating artery. In general, however, the stiffness is both less troublesome to the patient and less persistent than it is in cases of basal meningitis. In Case 22 (p. 287) all the muscles of the back of the neck became painful and stiff, and the patient complained of severe occipital headache after the rupture of an aneurysm on the left posterior cerebellar branch of the basilar artery. In Case 29 (p. 292) a ruptured aneurysm on the left anterior cerebellar artery caused a similar complaint of stiffness of the neck, and made the patient hold his head flexed upon the left shoulder in the pose characteristic of a cerebellar lesion of the left side. In Case 30 (p. 249) the first symptom of which the patient complained was a left-sided

cervical stiffness, accompanied by intense pain and tenderness of the left occipital region. During the next twenty-four days these symptoms persisted. After death an aneurysm, which had leaked and allowed blood to escape into the basal cisterns, was found on the left posterior communicating artery near the bifurcation of the carotid.

At the present time, in cases of meningitis, the only certain signs of an inflammation of the membranes covering the cerebrospinal axis is the finding of organisms or of cellular exudate and products in the cerebrospinal fluid; just so, in cases of hæmorrhage into the brain and spinal cord, the only certain proof that some vessel has ruptured is the finding in the fluid removed by lumbar puncture of blood-cells and pigment more or less uniformly intermingled with the cerebrospinal fluid. Moreover, it is found that if the blood has escaped from a vessel in the cranial cavity, the longer the fluid after lumbar puncture is allowed to run, the more blood-stained the specimen becomes; whereas, if at the time of the insertion of the needle damage is done locally to a vessel in the lumbar sac, the first few cubic centimetres of fluid collected are found to contain the greatest amount of blood pigment and the greatest number of cells. If the hæmorrhage is of recent origin, the cerebrospinal fluid shows bright red staining and little altered red blood-cells; later the colour becomes paler and yellower, and the red cells more broken up.

In Case 5, on the day of the seizure, the cerebrospinal fluid obtained by lumbar puncture showed much bright red staining and many little altered red blood-cells; at autopsy this blood was found to have escaped from a burst aneurysm at the junction of the left anterior cerebral and anterior communicating arteries. On the day of death the cerebrospinal fluid of Case 29 (p. 292) was found to be under considerable pressure and to contain a few red cells, an excess of polynuclear cells, but no organisms, and to be stained slightly with recent, little altered, blood pigment. The blood in this case had escaped from an aneurysm on the left anterior inferior cerebellar artery. In Case 30 (p. 249) the cerebrospinal fluid was examined on three occasions—fifteen days, eighteen days, and twenty-four days after the first seizure; on each occasion the fluid was under considerable pressure, and contained much blood pigment and many red blood cells; and on each occasion it was noted that the later specimens obtained after lumbar puncture contained more pigment than did those first collected.

As a point in differential diagnosis, it is noteworthy that in cases of cerebral aneurysm the vessel whose wall gives way lies in the meninges

outside the parenchyma of the central nervous axis, whereas in cases of direct rupture or of rupture into a cerebral or cerebellar neoplasm the vessel gives way in the substance of the parenchyma, with the consequence that in aneurysm staining of the cerebrospinal fluid occurs at an earlier moment, and before the leakage is so profound. Moreover, as Wichern has noted, the finding of blood-stained cerebrospinal fluid is more likely to be of aid in early diagnosis if the aneurysm occurs on one of the vessels of the posterior cranial fossa.

CHAPTER IV.—THE CLINICAL MANIFESTATIONS ASSOCIATED WITH THE DEVELOPMENT OF EMBOLIC INTRACRANIAL ANEURYSMS.

Clinically, cases of intracranial aneurysm of embolic origin fall into a different nosological group from those intracranial aneurysms of congenital and degenerative origin. In the embolic class clinical evidence of a state of septicæmia and general infection is usually present when the patient first comes under observation, and in the great majority of cases, as Church [8] first pointed out in 1870, evidence of cardiac disease, of the ulcerative or progressive type, has preceded the onset of the cerebral manifestations. Between 1907 and 1913 at the London Hospital thirteen examples of embolic cerebral aneurysms occurred, and in these a history of several attacks of acute rheumatism followed by the development of a condition of progressive endocarditis was obtained in seven cases (Cases II, III, IV, VII, VIII, X and XII) and at autopsy pathological evidence of infected endocarditis was also found in Cases I, V and IX. Case VI was one of pyæmia subsequent to a retropharyngeal abscess, Case XI was one of pyæmia where no primary focus could be determined even at the *post-mortem* examination, and Case XIII one of puerperal septicæmia with general pyæmia.

In two cases only (Case I, p. 293, and Case IX, p. 294) did the patients first come under observation at hospital complaining of nervous manifestations and in both before death signs of valvular disease of the heart were discovered, and in both in addition a history was obtained of indefinite aches and pains preceding by some days the onset of the hemiplegic seizure.

Blood cultures were taken in Case III on three occasions with negative results; the blood in Case IV yielded a Gram-negative diplococcus, in Case V a short-chained streptococcus, in Cases VII and VIII a streptococcus and in Case XI a staphylococcus. In the other seven cases no blood cultures were made.

In Cases VI and XIII the patients were extremely ill, and although under observation as in-patients at hospital, at the time of death no local cerebral lesions were suspected. At the autopsy in Case VI a thick-walled unruptured cerebral aneurysm was discovered on the left anterior cerebral artery, and in Case XIII two ruptured aneurysms on small cortical vessels were found. Case XI before death fell into a severe typhoidal state, and although meningitis was suspected and thought to be consequent on a pyæmic abscess, no localizing nervous signs were discovered; in this patient the *post-mortem* examination revealed an aneurysmal dilatation and blockage at the bifurcation of the basilar artery.

Ruptures of embolic cerebral aneurysms leading to apoplectic attacks in patients who did not realize that they were ill occurred in Case I, a small girl of 7, whilst playing in the street; in Case VII, a man of 31, in the street when returning from work; and in Case IX, a girl of 15, whilst helping with house work.

Case I (p. 293) was admitted unconscious to the surgical side and gave the signs of a left hemiplegia: she was at first thought to be suffering from a "fractured base," but on the discovery of mitral disease a correct diagnosis was made before her death, which occurred six hours after the apoplectic insult.

Case VII was found lying in the street unable to speak and paralysed down the left side of the body; he was brought up to the hospital by the police, where eighteen days later he died. The first attack of acute rheumatism in this patient occurred sixteen years before death, and during the two and a half years before the cerebral infarction, breathlessness, headache, and joint pains had been extremely troublesome. At the autopsy a ruptured septic cerebral aneurysm with thick walls, of the size of a cherry, beneath the inferior extremity of the right ascending parietal convolution was discovered.

The clinical history of Case IX (p. 294) is most illuminating. She was admitted to hospital with a right hemiplegia and total aphasia, but showing no signs of cardiac disease. Lumbar puncture yielded sterile blood-stained cerebrospinal fluid, suggesting that some vessel supplying the central nervous system had leaked. As an in-patient the hemiplegic weakness largely disappeared and the power of speech returned, but twenty-two days after the seizure signs of mitral disease were recognized and she began to complain of abdominal pain. During the next week she vomited frequently, wasted and became very anæmic. No definite abdominal signs were ever discovered and she died thirty-two days after

the initial hemiplegic seizure apparently from exhaustion. At autopsy a ruptured aneurysm of the coeliac axis artery ruptured into the lesser peritoneal sac, a thrombosed aneurysmal dilatation of the left renal artery, a thrombosed aneurysmal dilatation at the bifurcation of the left intracranial carotid artery and progressive endocarditis without cardiac hypertrophy were discovered.

In Case X, the patient was at home in bed when he suffered his first seizure, and in Cases II, III, IV, V, VIII and XII the first nervous manifestations occurred whilst the patients were under observation and treatment in hospital for progressive endocarditis. Case II, a man, aged 41, with an extremely large heart and ever-changing signs of mitral and aortic disease, had been in hospital fourteen days, when he woke at 7 a.m. one morning feeling weak and faint; at 7.30 a.m. he suddenly fell back in bed complaining of weakness of the right arm, became comatose and died thirty hours later from a ruptured septic aneurysm on the right anterior cerebral artery. Case III, a boy, aged 16, had been in hospital nine and a half weeks suffering from increasing myocardial weakness and pyrexia, when he was suddenly seized with acute pain in the left side of his head. He immediately lost the power of speech and became hemiplegic on the right side. Consciousness was soon lost, and one and a half hours after the seizure with signs of respiratory failure he died. At the autopsy a septic aneurysm of the size of three peas, which had ruptured, was found on a large temporal branch of the left middle cerebral artery. Case IV, a young man, aged 22, had been in-patient three and a half months and had suffered from many attacks of pain due to the infarction of the organs, when fifty hours before death he suffered a slight generalized convulsion, became comatose and died. At autopsy an unruptured septic aneurysm at the anterior superior angle of the island of Reil on a branch of the right middle cerebral artery was found. Case V came into hospital complaining of cardiac disease and pain in the left upper thigh; eight days before death he was suddenly seized with intense pain above the left orbit. This pain lasted acutely for a few hours, and five days later, accompanied by transient blindness of left eye which lasted a few hours only, returned. Fifty-six hours before death he became distressed, vomited, lost consciousness and developed signs of a left-sided alternate hemiplegia, paralysis of the left third cranial nerve and paralysis of the right face, tongue, arm and leg. Two septic cerebral aneurysms were found at the autopsy, a ruptured one on the left anterior perforating artery and an unruptured one on a branch to the parietal lobe of the left middle cerebral.

Case VIII, a girl, aged 16, after a three months' stay in hospital, suddenly became comatose and died three days later from a ruptured aneurysm on the right middle cerebral artery, without ever recovering consciousness. Case XII, a man, aged 36, had been fourteen days in hospital, when for some hours in the evening he became restless and excited, and after the attack was found to have a dilated left pupil which reacted sluggishly to light; nine days later on waking about 6 a.m. he became loquacious, restless, and complained of a roaring noise in his head; two or three minutes later he lost consciousness and when seen at 8 a.m. was comatose and showed evidence of right-sided cortico-spinal interference. Thirty hours after this seizure he died, and at autopsy a large ruptured aneurysm, 2.5 cm. in diameter, on the left middle cerebral artery at the end of the horizontal limb of the Sylvian fissure, was discovered.

After the rupture of the aneurysm on the right middle cerebral artery in Case I a spastic left hemiparesis, convulsive movements of the right extremities and conjugate deviation of the eyes alternately to right and left were noted. In Case II an apoplectic seizure due to the rupture of an aneurysm on the right anterior cerebral artery led to a complete paralysis of the right arm and weakness of the right leg, with signs of bilateral pyramidal interference, and a fixed dilated pupil on the right side. Case III had suffered since early childhood from weakness of the left external rectus muscle and middle ear deafness on the left side. After the rupture of the aneurysm on a branch of the left middle cerebral artery speech was lost completely and the right face, arm, leg, and right upper eyelid became paralysed. In Case V, after the seizure due to the rupture of a septic aneurysm on the left anterior perforating artery, the left upper eyelid was completely paralysed, the power of speech was lost and paralysis of the right face, arm and leg was noted. Case VII was first seen twelve days after the seizure; at this time he could utter some words distinctly but could not propositionize and got angry when he could not answer simple questions of which, apparently, he knew the answer. He could copy simple written characters and diagrams and made attempts to draw common objects; he could not copy sentences or printed words. He complained of right parieto-occipital headache. The left arm and left leg were paralysed and the movements of the left face, left half of the palate and tongue were impaired. Signs of cortico-spinal interference to the left half of the body were present and sensibility on this half was altered. Gradually these signs improved and the patient became able to repeat

any simple combination of words. Four days before death he developed a nocturnal psychosis with excitement and next morning speech was again limited to a few words, which, though constantly uttered and misused, could not be repeated on demand. From this time on, his general condition got worse and for thirty-six hours before death he was comatose. The rupture had occurred near the temporal pole from a branch of the right middle cerebral artery. After a seizure Case IX became hemiplegic on the right side, showed paresis of the right face, became unable to put out her tongue, and developed proptosis of the left eyeball and optic neuritis on this side.

The first seizure in Case X occurred nine days before the patient came under observation and was followed by weakness of the left arm and some difficulty with speech. When admitted to hospital two days after a second seizure he was unconscious, and exhibited a hypertonic left arm, a spastic left leg, a flaccid right arm and a hypotonic right leg, paresis of the left face and evidence of bilateral pyramidal interference; the right pupil was dilated, the left of medium size: neither reacted to light. He died without ever recovering consciousness seven hours later. At the autopsy a partially thrombosed and ruptured septic aneurysm of the size of a cherry-stone was found on the right middle cerebral artery 5 cm. from its origin.

In the paper quoted above Sir John Rose Bradford [4] remarks: "My point is that a patient may die from cerebral aneurysm which may have resulted from embolism, but that at the time of death you may not be able to find any gross evidence of its embolic 'origin.'" If Case IX (p. 294) had died shortly after her admission to hospital, certainly progressive endocarditis would not have been diagnosed, for between January 15 and February 6, 1911, repeated examinations of the chest by a series of competent observers failed to reveal any abnormal cardiac signs; no murmurs were present, she was not short of breath and the extent of the projection of the heart against the chest wall was certainly not increased. After the latter date, however, unequivocal signs of mitral disease appeared. At autopsy there was endocarditis of both the mitral and aortic valves, but the size of the heart was not increased.

In the cases of cerebral aneurysms due to infected emboli, apart from the characters of the hemiplegias as signs of localizing value we had in Case IX unilateral (left-sided) proptosis and optic neuritis; the unruptured aneurysm was found at the bifurcation of the left intracranial carotid artery pressing upon the left cavernous sinus. Case V was a good example of the alternate hemiplegia known as the Weber syndrome,

left-sided ptosis and paralysis of the right face, tongue, arm and leg. Case VII showed a characteristic interference with internal speech and apraxia of the right upper extremity; a ruptured aneurysm was found near the temporal pole on the main branch of the right middle cerebral artery.

Many authors have laid stress upon the appearance of subjective noises in the head; in Case XII alone of this series is any mention made of this manifestation. This patient, before he lost consciousness, complained of an intense "roaring in the head"; here a large aneurysm 2.5 cm. in diameter was found at the end of the horizontal limb of the left Sylvian fissure.

CHAPTER V.—SUMMARY OF CONCLUSIONS.

(1) The clinical and pathological findings in 44 new cases of cerebral aneurysm are described.

(2) From the point of view both of the clinical history and the *post-mortem* appearances, the cases showing at necropsy aneurysmal formations on the basal cerebral arteries fall naturally into two groups, the non-inflammatory and the inflammatory.

(3) In a series of 5,432 consecutive examinations of the head cerebral aneurysms due to non-inflammatory changes in the middle wall of an artery occurred in 0.57 per cent., and aneurysms due to inflammatory changes in the cerebral arteries associated with infective embolism in 0.24 per cent.

(4) In the non-inflammatory group degenerative changes in the walls of the basal cerebral arteries were often found associated with high blood-pressure, cardiac hypertrophy and evidence of general arterial disease, but in many of the cases there was no evidence of excessive blood-pressure either at autopsy or from clinical observations, and the general arterial degeneration and the degeneration of the cerebral arteries was no greater than in the average subject of the same age.

(5) In the non-inflammatory group a congenital weakness of the arterial wall at junctional points is an important factor in their formation.

(6) The proportion of aneurysms associated with infective embolism in the cerebral arteries to those in all the other arteries of the body was as 15 to 9.

(7) In this series of cases no example of a cerebral aneurysm due to, or associated with, an infection by the *Spirochæta pallida* occurred, but 96.2 per cent. of the aneurysms of the aorta, 100 per cent. of the aneurysms of the other elastic arteries, and only 6.25 per cent. of the

aneurysms of the muscular and small elastic arteries, to which class the arteries of the circle of Willis and the cerebral arteries generally belong, were consequent on the local weakening of the arterial wall due to the inflammatory reaction set up by the activity of the *Spirochaeta pallida*.

(8) Rupture of a cerebral aneurysm led to death in 0·44 per cent. of all cases of examination of the body, whilst direct rupture of an intracranial artery during the same period was the cause of death in 0·91 per cent.

(9) The largest aneurysm measured 30 mm. in diameter, but the great majority were much smaller.

(10) In 15 out of 31 cases (48·4 per cent.) of non-inflammatory cerebral aneurysms, whose ages varied from 53 to 19 years and averaged 38, no cardiovascular hypertrophy was present.

(11) The age-incidence of cerebral aneurysms of embolic origin is determined by that of progressive infective endocarditis and other chronic septicæmic and pyæmic conditions and is lower than in the non-inflammatory group.

(12) In 25 out of 31 cases (80·7 per cent.) of non-embolic aneurysm clinical manifestations attributable to cerebral hæmorrhage occurred; in 5 out of 31 (16·1 per cent.), no clinical manifestations of intracranial disease were recorded, and at autopsy an unsuspected and unruptured aneurysm was found; and in 1 case an unruptured aneurysm at the junction of the right carotid and middle cerebral arteries was found at the necropsy on a patient who for some time had suffered from frontal headache and had been deaf of his right ear.

(13) Amongst the cases which at autopsy showed ruptured non-embolic aneurysms two patients died before admission to hospital, and ten were admitted after a first apoplectic seizure and died without ever recovering consciousness.

(14) Multiple leakages of blood due to partial ruptures of the aneurysmal sac occurred in 13 out of 31 cases (41·9 per cent.). In these patients a history of multiple seizures of an apoplectic type occurred.

The clinical manifestations in this type of case form a definite nosological group rendering their diagnosis not difficult.

(15) The first rupture of the sac of a cerebral aneurysm was often brought about by a violent muscular effort or acute emotion.

(16) Before the aneurysmal sac ruptured signs of intracranial pressure were rare, but after this had taken place frequent; 10 cases out of 31 before death showed changes in the optic fundi.

(17) The headaches associated with non-embolic cerebral aneurysms have some localizing value.

(18) The interferences with intellectual and reflexomotor functions which occur in association with cerebral aneurysms, both before and after rupture, depend upon the site of the vascular deficiencies and the course which the hæmorrhage takes after rupture has occurred.

(19) The cranial nerves are frequently involved in blood-clot after rupture. Optic atrophy, bitemporal hemianopsia and lesions of the optic tract have been described, but the third pair of cranial nerves were those most commonly involved in this series of cases. Supraorbital neuralgia may be caused by pressure upon the Gasserian ganglion. In cases of aneurysms of the posterior fossa, and more especially of the cerebellar arteries, an involvement of the facial nerve after its exit from the pons was common. A subjective complaint of noises in the head occurred only in one case, and in this series no local affection in the posterior fossa of the ninth, tenth, eleventh, or twelfth pair of nerves was noted.

(20) After rupture of aneurysms of the posterior fossa, a complaint of stiffness of the neck is a sign valuable in diagnosis.

(21) The finding of blood cells and blood pigment in the cerebrospinal fluid is the only clinical proof of cerebral hæmorrhage; in ruptured aneurysms staining of the cerebrospinal fluid occurs early.

(22) Of 13 cases of aneurysms on the cerebral arteries due to infective embolism, 10 were associated with ulcerative, progressive endocarditis, and in 5 cases a positive blood culture was obtained, but in 2 cases the onset of nervous manifestations first caused the patients to seek admission to hospital.

(23) Rupture of the sac of an embolic cerebral aneurysm leading to cerebral hæmorrhage and the death of the patient occurred in 9 out of 13 cases.

(24) The localizing signs in cases of embolic aneurysms are usually scanty.

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APPENDIX.

(A) NON-EMBOLIC ANEURYSMS.

A case in which death occurred from the rupture of an aneurysm at the junction of the right anterior cerebral and anterior communicating arteries in a man aged 41, who had been under more or less continuous observation at hospital over a period of sixteen years, and had complained of recurring attacks of headache and been blind of an anæsthetic left eyeball for three years. The first seizure due to the rupture of the sac occurred forty-three days, a second twenty-five days, a third seven days, and a fourth twenty-six hours before death in coma.

Case 23 (32377/1903, 30306/1906, 30181/1909).—Edward C., aged 41, grocer, single, was admitted to the London Hospital under the care of Dr. Cecil Wall on January 21, 1909, and died on January 25. He had been under observation and in-patient at various times during the preceding twelve and a half years. In 1893, at the age of 25, he attended as an out-patient and was treated for "colic and left wrist-drop" with aperients, electricity, and liniments. At this time the case was diagnosed as one of "(?) plumbism"; under treatment his symptoms disappeared. In 1896 he was readmitted suffering from chronic diarrhœa; after seven weeks' treatment he was discharged relieved. From this time until his death he was subject to episodic attacks of diarrhœa and mælæna. In 1903 enteroptosis was diagnosed, and he was

treated with massage. In the full histories taken on these admissions no mention is made of any headache or abnormality of the left eye. Between 1902 and 1903 he suffered two attacks of hæmatemesis, and during the years 1896 to 1903 his weight varied greatly, between 11 st. 7 lb. and 8 st. 4 lb.; he stated that when his weight was low he was subject to attacks of diarrhœa and left-sided abdominal pain.

In January, 1906, he began to complain of headache, sleeplessness, and a feeling of confusion immediately after waking, in addition to his old symptoms of flatulence, attacks of diarrhœa alternating with periods of obstinate constipation and left-sided abdominal pain. A note made at this time states that he was blind of the left eye, following iridectomy for staphyloma, but does not give the date of the operation, and further states that the cornea of the shrivelled eyeball showed scars of old corneal ulcers. At this time no abnormal nervous signs were discovered; the heart was not enlarged and the cardiac sounds were clear. An explanation of his symptomatology was found in the profound enteroptosis and the finding of a right movable kidney and occasional albuminuria. The stomach was greatly dilated and prolapsed; when the patient stood erect the small intestines fell forwards and the hypogastrium bulged; the transverse colon could be moved vertically over a distance of 3 or 4 in. Under massage and hospital treatment his weight in sixteen days rose from 8 st. 4 lb. to 9 st. 1 lb. On discharge he was given an abdominal belt, and three months later reported himself as "free from all the old symptoms except the headache."

On December 12, 1908, forty-three days before death, he was seized with a "bad influenza"—dreadful headaches day and night, pains in the back of the head and neck, constipation, and vomiting. He remained in bed four days. During these days he retched frequently, his motions were loose and he complained of severe frontal and vertical headache. For the next two weeks he was constantly ailing; the headache never ceased, but he was able to attend to his shop. On December 31, 1908, twenty-five days before death, in the morning about 4.30 a.m., the headache became "worse than ever," he felt "really bad in himself," got out of bed and "started cursing everybody, using very foul language." After this attack until death he did no more work and complained of headache "always present but varying in intensity from day to day and hour to hour." On January 17, 1909, he suffered another exacerbation in symptoms. The pain in the head on this day seemed to begin in the back of the head just beneath the hairy region and shoot forward to between the eyes and "almost push my eyes forward." On the 19th he vomited several times quite apart from the intake of food, which he usually refused, and became extremely constipated. On the night of January 20 to 21 he became very excited, cried out for a knife with which to murder his wife, could not be kept in bed, and beat his children. He was given injections of morphia, and next morning admitted to hospital.

On admission.—The patient was a thin, anæmic man weighing 7 st. 8 lb. He was extremely irritable, resenting all interferences and exposure to light.

At times he was noisy and called for objects with which to commit murder on his relations. In a general way he was intelligent, talked freely and answered questions lucidly. He could not give any connected account of his actions and mode of life during the preceding weeks, but readily answered questions relating to his shop and previous admissions to hospital. He complained of much severe left-sided frontal headache and said that the pain was increased by pressure between the eyes. After admission he vomited frequently; the vomits were small, bile-stained and consisted almost entirely of altered and clotted milk; the vomitings bore no relation to the intake of food.

Speech was unaffected and attention feeble, his remarks fitting rapidly from thought to thought. There was no paralysis or weakness of any extremity. The grasps were equal and powerful. He complained of no spontaneous pains in the limbs and to testing no loss of tactile, painful or thermal sensibility was discovered. The answers to tests for the recognition of posture and passive movement were poor and defective compared with those obtained in other modes of examination. No trophic or vasomotor changes were noted.

The knee-jerks were glib and equal on the two sides. Ankle-clonus was not obtained. No plantar responses were obtained. The arm-jerks were natural.

The left eyeball was small and atrophic, and with this eye the patient could not appreciate light. The left fundus could not be seen; the right appeared healthy, and the edges of this disc were clearly seen and sharply defined.

There was definite ptosis of the right eye; this eyeball moved badly but no local weakness of any single muscle could be determined. Nystagmus was not present. The right pupil was small, regular in outline, and reacted normally to light and convergence. The movements of the face, jaw, tongue, palate and larynx were unaffected.

The patient suffered from retention of urine, and catheterization was necessary; the bowels were only opened after the administration of enemata.

The tongue was dry and the pharynx filled with dried mucus. The chest was long, flat, phthinoid, the intercostal spaces wide and oblique, the sub-costal angle narrow, and the costal margins everted; a Harrison's sulcus was present and the sternum was depressed. The neck was thin and the trapezii long and sloping. The apex-beat of the heart was felt in the fifth interspace in the mid-clavicular line. No murmurs were heard. There was no abnormal dulness over the lungs and the breath sounds were natural.

The abdominal wall was thin and the distance between umbilicus and pubes long; the outlines of the stomach which filled the epigastric and upper umbilical region could be seen, and splashing was easily elicited. The liver and spleen were not enlarged. The right kidney was easily felt and could be seized between the fingers. The urine contained a trace of albumin, but no sugar.

On the morning of January 24 the patient suddenly cried out, "Lift me up, it's coming again." A nurse rushed up to him and lifted him up; then he began to jerk his arms, head and legs. He did not bite his tongue. His

colour changed and the pulse became feeble and rapid. After about half a minute the movements became more violent, then general rigidity followed by a state of deep unconsciousness and snoring breathing set in. He remained stiff for some minutes and gradually fell into a state of heavy sleep. After the seizure he was found to have passed urine and fæces under him. During the next twenty hours he occasionally raised his right arm and waved his right hand or picked with it at the bedclothes. No absolute paralysis appeared, but the left arm became more flaccid than the right. On January 25, twenty-six hours after this seizure, he died of respiratory failure.

At the *post-mortem* examination made on January 26 (P.M. 87/1909), a ruptured aneurysm of the size of a currant-grape was found at the junction of the right anterior cerebral and anterior communicating arteries, from which blood had escaped, covered the frontal lobes, filled the superior longitudinal fissure and the basal cisterns, and had spread over the whole of the cerebellum. The frontal lobes were stained brown. The substance of the hemisphere around the aneurysm was softened and had allowed blood to escape into the lateral, and thence into the third and fourth ventricles. The brain weighed 1,545 grm. The left optic nerve and left eyeball were atrophic. In the aneurysm itself and in the other cerebral arteries no evidence of atheroma was obtained. A few small patches of atheroma were found in the coronaries, and in the aortic commissure and abdominal aorta there were one or two small plaques and in the femorals slight atheromatous changes, but the radials were neither thickened nor tortuous. The heart was not hypertrophied but the kidneys showed fine granular changes and a few cysts. The lungs, liver and kidneys were greatly congested. The contents of the small and large intestines were blood-stained. This blood had escaped from a sub-mucosal point in the first part of the duodenum.

A case of aneurysm of the left posterior cerebellar branch of the basilar artery which at autopsy was found to have ruptured and given rise to a mass of blood-clot which compressed the pons, cerebellum, medulla, and the occipital lobe of the left cerebral hemisphere in a married woman, aged 42, who, when aged 25, and eight months pregnant of her second child, had suffered a transient hemiplegia affecting the right face, tongue, arm and leg, and who for five months before death had complained of slight epileptiform (petit mal) attacks with visual sensations. Nineteen days before death this patient had a seizure, followed by a second twelve days and a third ten days before the fatal issue. On admission to hospital, delirium, paresis left face and right hemiplegia of arm and leg, tenderness in left occipital region and stiffness of the upper part of the neck, left cerebellar posture of head, no nystagmus, early optic neuritic changes right.

Case 22 (43124/1909).—Anne S., aged 42, married, was admitted to the London Hospital under the care of Dr. F. J. Smith, on November 19, 1909, and died on November 24. She married in 1885, and had had two children and no miscarriages. No history suggesting primary or secondary syphilis

could be obtained. In 1889, at the age of 22, left inguinal colotomy for "stricture and ulceration" of the rectum was performed at St. Mark's Hospital. This stricture was thought to have had syphilitic origin. At the age of 25, when eight months pregnant of her second child, she suddenly woke one morning to find the right half of her body—face, tongue, arm and leg—paralysed and some difficulty with speech. The face and speech rapidly improved, and before her baby, which is still alive and now a healthy young woman, was born, the weakness of the extremities had largely disappeared. During the years 1892 to 1908 her health was good.

Between June and November, 1909, the patient had suffered five or six attacks of "blindness lasting a few minutes." In these attacks she never lost consciousness, and after ten minutes or so seemed perfectly well. The attacks were not accompanied by any headache, and in them she never vomited.

On November 5, 1909, nineteen days before death, she was seized with a sudden severe pain in the head and a sensation as of a "pulling of the back of her head as if her head were in a vice." This severe pain in the occipital region was accompanied by "aches all over." After the attack the left half of her face became "funny and weak." On November 12, she suffered from another "turn" in which she vomited once and became very "queer" and "quiet." On November 14, she suffered a second seizure "exactly like that on the 5th." The headache at this time was severe and her neck became "fearfully stiff and tender." After the headache ceased she was drowsy and suffered from "fever." With these attacks no weakness of the extremities was noticed.

On admission, the patient was an obese woman, weighing 13 st. 2 lb., who looked old for her years. She lay in bed moaning and groaning, and absolutely helpless. Shortly after admission delirium with outbursts of loud, frequent shouts of foul and filthy language set in. She mistook the people around her for her own relatives, and abused them. She was suspicious, but at times would listen to reason, and could with persuasion be got to answer questions. On command, simple orders were carried out. She complained of pain and tenderness over the region of the left occiput and nape of the neck, and greatly resented all attempts at turning her head. The head was held strongly flexed with the chin pointing towards the left. Under observation, she did not vomit, nor did she exhibit any irregular, involuntary movements.

The right arm and leg were spastic and paretic. All movements on this half of the body were slowly carried out and clumsily performed. No sensory loss was discovered. The right knee-jerk was exaggerated, the left could not be obtained. Ankle-clonus was not elicited. On the right side the plantar response was extensor, on the left flexor. The arm-jerks on the right side were brisk, on the left only doubtfully obtained.

The left fundus appeared healthy. On the right side the veins were engorged, the arteries unaffected, and the edges of the pink disc indistinct and blurred. Hearing was not affected.

Ocular movements were natural. Ptosis and nystagmus were absent. The

pupils were small, regular in outline, and reacted definitely, though sluggishly, to light. The left face was paretic in its lower half, but moved fairly in emotion. The tongue could be protruded straight and held steadily. The sphincters were under control.

The rate of the pulse varied between 96 and 120. The temperature was raised to 103° F. Respirations were shallow—36 per minute. The tongue was thickly furred. The chest moved naturally. The heart was not enlarged and the cardiac sounds were natural. In the left inguinal region was an old colotomy wound, with healthy appearance. The liver reached below the costal margin, and its edges could just be felt. The urine contained neither albumin nor sugar.

On the nights of the 20th and 21st the patient became wildly delirious and excited. Next morning she was comatose, and the right side of the face was seen to be paretic. After this the pulse began to fail, and became variable in force and rate, tending to about 88 per minute. On the 22nd she could be roused with difficulty, cried out repeatedly, understood apparently some commands, and at times uttered a feeble unintelligible reply. Death occurred with increasing coma, grouped rhythmic respirations, flushing and cyanosis of the face and hyperpyrexia (T. = 105·6° F.) on the morning of the 24th.

At the autopsy (P.M. 1166/1909), performed on November 25, a ruptured aneurysm on the left posterior cerebellar branch of the basilar artery was found. The middle peduncles of the cerebellum, the pons, and the medulla oblongata were compressed on the left side by a lump of firm, brown-pigmented clot, and the meninges around this mass of clot were deeply stained, and of a red-brown colour. There was no softening of the brain, which weighed 1,134 grm. No evidence of atheroma was found either in the aneurysm or in the other cerebral arteries, but in the arteries of the general circulation moderate atheromatous changes were seen as fatty and calcareous plaques scattered here and there over the aorta, coronaries, &c. The heart weighed 361 grm. The lungs showed severe acid digestion and acute purulent bronchitis of the lower lobes. Two and a half inches above the anal orifice was an impervious stricture of the rectum, for the relief of which a permanent colostomy had been made; below this opening the mucous membrane of the colon and rectum was contracted and atrophied.

A case in which the partial rupture of an aneurysm at the junction of the left anterior cerebral and anterior communicating arteries occurred suddenly in man, aged 53, whilst watching a football match. Attacks of drowsiness and delirium, epileptiform seizures, clumsiness in movements, left frontal headache, left optic neuritis. Death on twenty-seventh day.

Case 16.—30191/1911: Joseph M., aged 53, married, was admitted to the London Hospital under the care of Dr. Francis Warner on January 26, and died on February 4, 1911. He had followed the trade of carpenter for thirty-five years, and until the onset of the illness from which he died

had enjoyed good health. He married at the age of 26, was a widower, and by his wife had had five children, four of whom survived, aged respectively 25, 23, 21, and 19 years. He denied venereal infection and exposure. In early life he had had attacks of "typhoid" and "typhus" fevers; in recent years he had suffered on three occasions from "influenzal colds with fever and pains in the back."

During the latter part of December, 1910, and the first days of January, 1911, he had been feeling particularly well. On January 7 he went to watch a football match, and, whilst looking on, "came over queer, shivered, and developed severe frontal headache." He was taken home in a cab and put to bed. Consciousness was not lost; vomiting set in some hours later on the same day; he vomited several times, and brought up large quantities on each occasion. With the headache and vomiting he himself became irritable and ill-tempered. The pains in the head were chiefly vertical and frontal. He remained in bed at home from the 7th until the time of admission, complaining of a persistent headache of varying intensity; whilst in bed at home he vomited on several occasions, and was very constipated. Suddenly on the night of the 12th he became noisy, talkative, and delirious, saw black objects before his eyes, and made attempts as if to seize them. Next morning he was better again, and seemed "his normal self." A few days later, however, he began to "talk strange, and behave as if not right in his mind," but at the same time slept well. On January 19 he suffered from his first "fit"; in it he threw himself about, opened and shut his mouth repeatedly, and turned his eyes upwards. On the nights of the 20th and 21st he had three such attacks, "lasting on him altogether two hours and a half." On admission his daughter said that he had not recognized anybody since the 22nd, and had passed his urine and motions into the bed since the 24th. A letter from his doctor stated that albumen had been present in the urine on the 7th.

On admission, the patient was a well-preserved man, aged 53, of healthy appearance. He was dazed, drowsy, and lethargic. In answer to questions, he usually gave some reply after a pause, but the reply was pointless and irrelevant, rather than incorrect. He could give no connected account of himself, and when asked who he was, where he lived, or how long he had been ill, merely uttered some incomprehensible sounds. Apparently hearing was not affected. Attention after he had been roused was fleeting. He took no interest in his surroundings, and in general lay vegetable-like. Spontaneous movements of the hands were occasionally seen, but of the face and legs rarely. He showed evidence of recent wasting, was dusky and cyanosed; his face was expressionless and drawn. The mouth usually remained half-opened, exposing an extremely harsh brown tongue. The lips were dry and the pharynx filled with mucus. The fairly preserved teeth were covered with sordes and dried secretion. The skin was harsh and dry, and cedema was not present. Large varicose veins coursed over both lower extremities, and pigmentary scars, apparently secondary to old and healed varicose ulcers, were seen on the front of the shins. No suggestion of syphilis was discovered.

The apex-beat of the heart was felt in the fifth interspace, a quarter of an inch outside the mid-clavicular line. The area of superficial cardiac dullness was small. The clavicles were raised, the sternum fixed, the chest barrelled, and the respiratory movements small. No abnormal dullness was found over the lungs. The breath sounds were feeble and distant, and expiration was prolonged. No abnormal cardiac bruits were heard. The rate of the pulse was 96 per minute; before death it fell to 66. The temperature was slightly raised, to 99.5° or 101° F. throughout the illness. The superficial arteries were tortuous and felt thickened. The blood-pressure, as measured by the Riva-Rocci apparatus in the right brachial artery, was 180 mm.

The liver was not enlarged and its edge could not be felt. The splenic dullness was not large and the lower pole was not palpable. No abnormal signs were found in the abdomen. The urine contained albumin and a thick cloud was obtained on boiling. The specific gravity varied from 1028 to 1030. On standing a thick deposit of amorphous urates was obtained. Sugar was not present.

On the three days preceding death, February 1, 2, and 3, the patient exhibited several epileptiform attacks; the movements chiefly affected the left upper extremity and were followed by loss of consciousness, dilatation of the pupils, and the disappearance of the corneal reflex. Each attack lasted from a half to two minutes and was accompanied by relaxation of the sphincters. After the attacks he sank into a quiet and drowsy state. Headache was a constant complaint and was referred to the left temple and above the left orbit. As an in-patient he did not vomit.

There was no absolute paralysis of any limb. Irregular, inco-ordinate, clumsy movements of both hands occurred from time to time. Spasticity was not present and the tone of the muscles was little altered. Sensation was difficult to test, but no loss could be determined. Dermatographia was easily elicited.

The knee-jerks were exaggerated, the response on the right side was somewhat brisker than on the left. Ankle-clonus was not obtained. The arm-jerks were brisk. On both sides the plantar reflexes gave a flexor response. The abdominal and cremasteric reflexes were just obtained. The left corneal reflex was readily elicited, the right only doubtfully obtained.

The right optic disc and fundus appeared pale, the veins were full, but the arteries small and the edges of the disc sharp. On the left side the disc was swollen and its edges blurred; the veins on this side were larger than on the right but the arteries appeared fairly normal. The drums of the ears appeared healthy.

Ptosis and nystagmus were absent and ocular movements free. The pupils were equal and reacted sluggishly to light. Facial movements were rarely seen, but no paralysis could be made out. The movements of the tongue, larynx and palate were unaffected.

The patient suffered from retention of urine and dribbling overflow incontinence. He was constipated and the bowels were only opened with

enemata. Death occurred from respiratory failure on February 4, twenty-seven days after the first seizure.

At the autopsy (P.M. 104/1911) performed on February 4, a ruptured cerebral aneurysm, of the size of a pea, was found at the junction of the left anterior cerebral with the communicating arteries. Around the aneurysm was much hæmorrhagic matting of the meninges. All the cerebral ventricles were filled with blood-clot which had found an entrance through into the left lateral ventricle by local softening and erosion. At the base of the brain was much intradural and intraarachnoid hæmorrhage. The brain weighed 1,535 gm. There was no visible atheroma of the cerebral arteries, but slight atheroma was seen elsewhere, a few fat-flecks in the coronaries, and pin-head fat-flecks in the commissure and descending aorta. The weight of the heart was 290 gm. The lungs were emphysematous and showed a fibro-calcareous nodule at the apex of the left lung and a few smaller nodules in the right upper lobe. The other organs appeared healthy.

On microscopic examination the aneurysm was found to have a thin wall made up of fibrous tissue with some slight fusiform thickenings. Some of these thickenings appeared to be fibrosed muscularis, others fibrotic thickenings of the intima in which a few elastic fibres were seen.

A case in which the rupture of an aneurysm of the left anterior cerebellar artery led six days later to the death of a young man, aged 22. Drowsiness, left facial paralysis, bilateral corticospinal interference, left cerebellar posture of head, stiffness of neck and blood in the cerebrospinal fluid.

Case 29 (32669/1909).—Arthur P., aged 22, stable-boy, married, was admitted to the London Hospital, under the care of Dr. Leyton, on November 24, 1909, and died on November 25.

His father stated that his health had been good until November 19, 1909. In 1903 he had been laid up in bed at home for six weeks with "rheumatic fever," and in 1907 he suffered an attack of "gonorrhœa." On November 19, while in the stable he fainted, but after the faint did a full day's work, going a complete round with the cart. On the 20th he refused his food, said he "felt queer" but made no specific complaints. On the 21st he got up but was "half-asleep, talked to himself, and would not listen to what was said." On the 22nd and on the morning of the 23rd he seemed better, but about 11 a.m. on the latter day he had a seizure. At the time he was walking about the house, when suddenly he reeled, came over stupid and deaf. He was put to bed and when found at 5 p.m. was deeply unconscious. A doctor was called and shortly after midnight he was admitted to hospital.

On admission, he was semi-conscious and in general lay quiet in bed on his left side. He resented all interference and when spoken to made some unintelligible replies, continuing thereafter to mumble to himself. His face was flushed, his breathing stertorous. On the bridge of the nose was a scar obtained in his fall on the 19th. The right side of the heart was dilated but there was

no evidence of any enlargement of the left ventricle. At the apex a systolic murmur was audible. With the exception of a few rhonchi, no abnormal signs were discovered over the lungs. The urine contained a trace of albumen but no sugar and no casts. The temperature varied between 101° and 102° F., the rate of the pulse from 92 to 116 and of respirations from 32 to 38 per minute. The blood-pressure in the brachial artery measured 110 mm.

The optic discs and fundi appeared healthy. All the ocular movements and the movements of the pupils were unaffected, but the patient could not be persuaded to fix his gaze upon any object. The left side of the face both in its upper and lower halves was paralysed. The tongue could not be protruded.

Both arms were held stiffly, the right more so than the left. The left arm from time to time twitched in an irregular manner. The right leg was paretic and the tone in its muscles increased. There was no rigidity of the muscles of the neck but the head was held flexed towards the left shoulder and the chin pointed towards the right. Sensation could not be tested.

The knee-jerks on both sides were exaggerated, ankle-clonus was elicited from both ankles, and the response from the plantar reflex on each side was extensor. Both wrist- and elbow-jerks were brisk. The abdominal reflexes could not be obtained. Urine and faeces were passed incontinently.

Consciousness was never regained. On the 25th the eye-movements were more dissociated and irregular and the head more definitely rotated to the left; true nystagmus, however, was not obtained. Intense photophobia was present. The reflexes varied, at times ankle-clonus was readily obtained, at other times this sign was absent. On the 25th lumbar puncture yielded clear fluid under pressure which contained a few red cells, excess of polynuclear cells, but no organisms. Death occurred six days after the initial "faint" on November 25 from respiratory failure.

At the autopsy (P.M. 1166/1909), a ruptured aneurysm of the size of a pea was found on the left anterior inferior cerebellar artery. All the other cerebral vessels appeared healthy, there was no cardio-vascular hypertrophy and all the organs except the lungs, which showed broncho-pneumonic changes, appeared healthy.

(B) EMBOLIC ANEURYSMS.

A case of infected endocarditis in a child aged 7 years, in whom, after a period of slight malaise, death occurred from cerebral hæmorrhage seven hours after a seizure consequent upon the rupture of an embolic aneurysm on the right middle cerebral artery.

Case I.—20861/08, Bessie G., aged 7, was admitted to the London Hospital under the care of Mr. Percy Dean on April 7, 1908, and died seven hours after admission.

The mother stated that the child had been ailing for some days but had never been really ill until the day of admission. On this day, whilst playing on the stairs, she suddenly fell down four steps and struck her forehead against

the stairs. Immediately after the accident she was brought up to the hospital and admitted.

The patient was a well-developed child of 7. On admission she was unconscious. At intervals she showed irregular movements of the right upper and lower extremities; in these attacks the eyes were observed to roll slowly outwards, first to the left and then to the right, and the mouth was seen to twitch in an irregular fashion. The left upper and lower extremities were paralysed and stiff.

Both knee-jerks were brisk. On the left side the plantar reflex gave an extensor response, on the right a flexor.

The area of cardiac dulness was increased to the right of the sternum, but the apex-beat was not displaced either outwards or downwards. At the apex the first cardiac sound was replaced by a long, blowing, systolic murmur which was well heard in the axilla. The pulmonary second sound was accentuated. No abnormal physical signs were discovered in the lungs and no signs of any injury were present. The rate of the pulse was 68 per minute and of respiration 27 per minute, and the temperature was 96° F.

Chloral was administered to the patient by the mouth, but five hours later respiration began to fail. Artificial respiration was carried on for half an hour, at the end of which time the pulse could no longer be felt at the wrist.

At the autopsy performed on April 8, 1908 (P.M. 345/1908), a ruptured aneurysm of the size of two peas was found on the right middle cerebral artery about 1½ in. from its origin. The posterior part of the basal ganglia and the internal capsule had been almost completely destroyed and blood-clot was found in both lateral and in the third and fourth ventricles, whilst the convexity of the right cerebral hemisphere was covered with sub-arachnoid hæmorrhage. The heart, which weighed 113 gm., showed the appearances of progressive endocarditis, with large fibrinous vegetations on the mitral and aortic valves. The spleen was septic and the organs engorged. No other aneurysms or infarcts were discovered. Microscopic examination showed that the aneurysm was filled with organizing blood-clot and that the aneurysmal wall exhibited an area of necrosis with much round-celled and purulent infiltration around the artery.

A case of infected endocarditis with multiple infarctions and the formation of embolic aneurysmal dilatations on the left intracranial carotid, the left renal and the celiac axis arteries in a girl aged 15. Onset of acute manifestations with a seizure followed by aphasia and right hemiplegia thirty-two days before death: cardiac affection first recognized seven days before death, which occurred in consequence of bleeding into the lesser sac of the peritoneum.

Case IX.—40136/1911, R.H.—Mary N., aged 15, was admitted to the London Hospital under the care of Dr. Robert Hutchison, on January 15, 1911, and died on February 15.

As a baby the patient had suffered only from attacks of whooping-cough

and measles. She had never suffered from acute rheumatism or scarlet fever and had had good health until the onset of the illness for which she was admitted to hospital. About four weeks before admission, her mother stated, she had had a blow upon the head. This blow was not followed by untoward symptoms, but from it her mother dated the present illness. On January 8, 1911, the patient began to complain of indefinite aches and pains in her arms, legs and back; they were, however, slight, and she was not confined to bed. On January 14, the day before her admission, she had a seizure. She fell down, clenched her teeth and voided urine and fæces. The seizure was followed by a period of restlessness marked chiefly by irregular movements of the left arm and left leg. After the seizure until the time of her admission she never spoke.

The patient was a fairly well developed Hebrew girl of 15, with dark hair. She was not anæmic and the lymphatic glands were not enlarged. She was drowsy, irritable, and only moved when stimulated or in response to loud noises. No wounds were discovered on her head or body. The cheeks were flushed, more especially on the side of the face on which she had been lying. Erythematous patches were seen at all points of pressure.

The right arm and right leg were paralysed; the right arm was stiff, the right leg flaccid. High-grade movements of a choreio-athetotic type of the left hand occurred from time to time. The left leg was moved freely, apparently under volition.

The right knee-jerk was exaggerated and knee-clonus was obtained on this side; on the left side the knee-jerk was readily obtained, but was not exaggerated. No ankle-clonus could be obtained. On the right side the plantar reflex gave an extensor response, on the left a flexor. On the right side no abdominal reflexes could be obtained, on the left they were brisk. The elbow-jerk and wrist-jerk on the left side were normal, on the right these could not be elicited. The jaw-jerk was normal.

Sensation could not be tested. The right arm was blue and cold, the left of normal appearance.

The right optic disc appeared healthy, but the edges of the left were blurred and the whole fundus on this side had a ground-glass appearance. The drums of both ears appeared healthy.

Ocular movements were well carried out. The right eyeball appeared more sunken than the left. The pupils were equal, of moderate size and reacted briskly to light. The lower half of the right side of the face and the levator palpebrarum on this side were parietic. The tongue could not be protruded. The head was rotated slightly to the left and the sternomastoid muscle on the right side appeared to be completely paralysed.

The patient was constipated and the bowels only moved after the administration of enemata. Urine was passed incontinently.

On admission the rate of the pulse was 120 per minute; the beats were regular and equal. The apex-beat of the heart was seen and felt in the fifth space just inside the mid-clavicular line. At all the areas both cardiac sounds

were heard and no murmurs were present. The pulmonary second sound was slightly accentuated. The rate of respiration was 24 per minute. The movements of the chest were unaffected and the breath sounds were unaltered. The abdomen was somewhat sunken. Neither the liver nor the spleen could be felt, and the urine contained neither albumen nor sugar. The lips were dry and the tongue coated with a brownish fur. The tonsils were large.

The temperature on admission was 100° F. The temperature for eight days after admission was raised and somewhat irregularly hectic, ranging between 101° in the evenings and 99° in the mornings. On the three days before death after an apyrexial period, the evening temperature rose, and on the evening of February 13 reached 102° F.

On January 16 lumbar puncture was performed and 30 c.c. of cerebrospinal fluid were withdrawn. This fluid contained many red blood corpuscles, a few lymphocytes and a large excess of polynuclear cells. On January 26 lumbar puncture was again performed; the fluid on this date was under pressure, but on centrifugalization it yielded no cells and cultures made from it proved sterile.

Ten days after admission the patient began to talk again, and the right hemiplegic weakness commenced to clear, and until about February 6 the patient seemed to be making a good recovery; on this day the patient vomited and the first cardiac sound became much weaker. On February 8 a loud mitral systolic murmur was heard for the first time. After this date the patient became more ill, wasted, refused food and gradually sank, apparently from exhaustion and increasing anæmia. Death occurred on February 15, thirty-two days after the initial seizure.

At the autopsy performed on February 15 (P.M. 137/1911), an aneurysm, 3 cm. in diameter, partially walled with blood-clot, was found on the celiac axis artery. This aneurysm had ruptured into the lesser peritoneal sac. The peritoneal cavity contained 595 gm. of blood-clot and 1,136 c.c. of serous fluid. The heart, which weighed 141 gm., showed a condition of ulcerative endocarditis, there being one large slimy, polypoid and many small granular vegetations on the mitral valve. In the hilum of the left kidney the left renal artery was found dilated and thrombosed; this thrombosis had given rise to a total infarction of this kidney. The right kidney showed a condition of acute hæmorrhagic nephritis. The spleen was septic and weighed 169 gm., and the liver showed much parenchymatous degeneration.

At the point of bifurcation of the left intracranial carotid artery was a thrombosed aneurysmal dilatation caused by a septic embolus. The left basal nuclei and the adjacent part of the left centrum semi-ovale showed white and yellow softening, and above the posterior limb of the fissure of Sylvius was an area of central softening measuring 3 cm. in diameter.

DEGENERATION OF MUSCLE FOLLOWING NERVE INJURY.

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INTRODUCTION.

As the result of the large number of cases of nerve injury caused by the present war there has been a remarkable revival of interest in the study of the electrical reactions of denervated muscle. Two years ago, in this country at any rate, few physicians had any accurate knowledge of the subject and this for two reasons, first because injury to peripheral nerves is comparatively rare in civil life and second because in those diseases which are associated with degenerative changes in the muscles routine electrical examination was in the great majority of cases neglected. It is not too much to say that not one student in a hundred had at the time of passing his final examination anything more than the crudest notion of the differences between the electrical responses of a healthy muscle and those of a muscle paralysed by anterior poliomyelitis. At the present day, however, with the presence of thousands of wounded men in the country, this hitherto obscure branch of medicine has leapt into prominence. At no time has a knowledge—and by that I mean a widely-disseminated knowledge—of the elements of electrotherapeutics been so important. To the modern military hospital the electrical department has become as essential a part as the X-ray room.

Many medical men have had to learn the principles of the subject from the beginning, while others who had had previous experience have discovered numerous fallacies in the older teaching. My object in the present paper is to review the present state of our knowledge of the subjects, to put on record fresh observations, and to explain the phenomena as far as possible on rational grounds.

CHAPTER I.—HISTORICAL SKETCH: ERB'S SCHOOL.

If we study the history of medicine we find that in cases where one man has possessed knowledge far exceeding that of any of his contemporaries, or has written far more on the subject than anyone else of his time, the tendency is for future generations to accept the teaching of the master as tradition, to ignore the conditions in which he worked, and to neglect to subject his work to the scientific criticism and experiment made possible in later years. A classical instance of this is seen in the way in which the deification of Galen retarded the development of anatomical knowledge for several centuries until the time of Vesalius. Similarly with the branch of medicine now before us—electromyology as it may be called. The dawn of our knowledge of the subject is associated pre-eminently with the name of Erb, who discovered and collected a mass of information bearing upon the change which a muscle undergoes when its motor nerve is divided. And we find that later neurologists have come to regard the name of Erb almost with a reverence like that with which the dissectors of the middle ages regarded the name of Galen.

Now whether we agree or not with the facts laid down by Erb, we must acknowledge the thoroughness with which he and his school investigated the problem. In spite of the great development of electrophysiology in the last forty years our clinical knowledge has advanced comparatively little. Instead, the clinical phenomena have come to be regarded merely as signs, useful for diagnostic purposes, but of an empirical nature, while few attempts have been made to explain them on rational grounds.

The first hint of changes in the electrical responses of muscles after injury to their nerves came from Hallé, of Paris, as early as the end of the eighteenth century. The significance of this discovery, however, was not realized: the time was not ripe and the question lay dormant again for about sixty years. In the middle of the last century came the rapid

growth of the continental school of physiology. It was a time when the electrical phenomena of living matter aroused the greatest interest among biologists. It is not surprising therefore that physicians began to turn their minds in the same direction. To Remak [25] belongs the credit of being the first to revive the forgotten work of Hallé; Neumann showed that a degenerated muscle had lost the power of contracting to a stimulus of momentary duration, while Baierlacher [2] appears to have been the first to give a practical demonstration of clinical cases. In 1859 the last-named showed a case of Bell's paralysis where the muscles gave no response to faradization but were hyperexcitable to the constant current. In 1868 two papers appeared simultaneously, the first by Erb [8], embodying the results of his clinical investigations on man and his experimental work on the rabbit, and second by Ziemssen and Weiss [29], who came to the same conclusions experimentally as Erb. In the following year Brenner confirmed Erb's clinical findings.

In 1874 [9] Erb wrote his classical account of the phenomena. As this account formed the basis of all future work we may give a brief summary of it.

In the first place Erb insisted upon the difference between the changes undergone by nerve and those undergone by muscle. Changes in the former are thus described. Two or three days after section the irritability to the faradic current may be increased; after this the excitability to both faradic and galvanic current diminishes simultaneously, and in seven to twelve days the nerve is totally inexcitable. The change begins at the site of the lesion and spreads peripherally. Return of irritability resembles loss in that it affects both forms of current simultaneously, the process beginning at the lesion and spreading peripherally. The excitability of the nerve remains for a long period subnormal even when there is full voluntary power. In the early stages of recovery there is a period when voluntary power is present, while at the same time the nerve is inexcitable below the lesion but excitable above it—this corresponds to a period histologically when the myelin sheath is either wanting or is incompletely formed.

The changes which muscle undergoes are quite different. Response to faradism diminishes at about the same rate as in nerve, being lost during the second week. This however is true only for stimulation through the skin. Direct stimulation of the bare muscle gives a limited contraction of the subjacent fibres for a long time after the injury. Recovery of faradic irritability usually occurs later than in nerve, remaining subnormal for a considerable period afterwards.

To the constant current muscle becomes less excitable in the first week. In the second week there is a distinct hyperexcitability accompanied by a qualitative change. The contraction which was previously short and brisk is now long and sluggish. Moreover, the muscle becomes increasingly sensitive to the anodal closure current (A.C.C.), so that the anodal closure becomes as effective as the kathodal closure (A.C.C. = K.C.C.) and occasionally ("nicht selten") the A.C.C. preponderates. A similar alteration affects the opening contraction. The muscle may even remain in tonic contraction during the passage of the constant current. When these changes have reached a certain stage, the opening contraction diminishes and, according to Brenner, in the same proportion as the increase of sluggishness and the decrease of irritability to currents of short duration. This stage lasts from three to eight weeks, often longer.

Following this is a second stage characterized by a progressive diminution of excitability to the constant current, a further preponderance of the A.C.C. over the K.C.C., and an increase in the sluggishness of contraction. This is contemporaneous with a gradual disappearance of the cross-striation. Finally a weak A.C.C. is the only "sign of life."

But if regeneration takes place the normal reactions gradually return, but the period during which the excitability is still subnormal may in bad cases be very prolonged.

The return of excitability in muscle is quite independent both of the return of voluntary power and of the regenerative process in the nerve.

A stage can be recognized at which the nerve is undergoing regeneration while the reactions of the muscle are still unaltered—moreover, the clinical picture varies with the rate at which the recuperative process occurs. If regeneration occurs early, normal excitability of the nerves may be co-existent with an abnormal response in the muscle. If the process is later in appearing we have the syndrome of diminished excitability of the nerve with the presence of qualitative changes in the muscle.

Erb also mentions the increased mechanical irritability of the muscle which he says occurs *pari passu* with the heightened excitability to the galvanic current.

A full account is also given of the corresponding histological changes. It is sufficient here to note that he believed in the view then universally held that regeneration of nerve originated peripherally.

The increased irritability of muscle to the constant current corresponds to the period of proliferation of the nuclei of the muscle cells, while the later stage corresponds to the atrophy of the muscle fibres. The slow recovery of the muscle as compared with that of the nerve he believes to be due to the mechanical obstruction afforded by the development of fibrous tissue.

It would not be necessary thus to quote in extenso Erb's teaching were it not for the fact that with the course of years the exact knowledge which existed forty years ago has gradually been forgotten, and all that has percolated into the average text-book of neurology of the twentieth century is the bald statement relating to loss of faradic excitability and polar reversal, the latter expressed in the dogmatic form A.C.C. > K.C.C. Further, many facts which we have quoted above have recently, through ignorance of the early work, been resuscitated and served up as modern discoveries.

On the whole Erb's account met with general acceptance. But there were not wanting those who disagreed on certain points. Of the opponents, most prominent was Vulpian, who dissented from Erb on two grounds, first on the question of the hyperexcitability of muscle to the constant current, second to the predominance of the A.C.C. over the K.C.C. It is in answer to these objections that Erb made his often quoted and often misquoted statement that "he knew scarcely any sign so certain and free from error as the heightened irritability to the constant current and the qualitative changes in the contraction."

The unquestioning acceptance with which Erb's thesis was received in this country is shown by a perusal of Hughes Bennett's work on Medical Electricity [3]. The account which is there given of the signs of degeneration is practically a verbatim report of Erb's account which is summarized above.

On the physiological side Erb's account of the reversal of polarity was received with profound suspicion. As early as 1867 Aeby [1] had shown reversal of polarity in the fatigued frog's muscle. Engelmann, though he at first criticized the experiment, was afterwards forced to admit that the phenomenon could occur. Biedermann, however, was entirely sceptical, believing the results to be due to the secondary anodal and kathodal points inevitable when strong currents are used. Writing in 1894 he says: "Before giving a final judgment it would be necessary here . . . to make further investigations with unassailable methods, for the conditions under which alone experiment can be tried in man, or have been tried in other animals, by no means correspond to the

demands of an exact physiological method. On the other side there are so many results, derived from irreproachable experiments upon different muscles and nerves which are opposed to a theory of reversal of polar effects that any supposed exception must *a priori* encounter suspicion, and can only hope for recognition of the conditions of experiment, and all accessories are perfectly simple and obvious" [4].

In attempting to criticize Erb's work in the light of modern knowledge there are certain points which must be borne in mind. That was a time when electrical apparatus was not to be compared in point of accuracy with that which is available at the present day. It is unfortunate, too, that in his original paper Erb gives no accurate account of the method which he employed. It is clear, however, that he measured the current by the number of Daniell cells in series from which the current is derived—a method open to obvious fallacies. His method of estimating the amount of contraction is indefinite; a slight contraction appears to have been represented by the sign Z, a slightly larger contraction by ZZ, and so on up to ZZZZZ. Ziemssen and Weiss, who give some account of the apparatus which they used, seem to have worked, generally speaking, on the same principles. It must be remembered, too, that these discoveries were made before surgery had been revolutionized by Lister. Operations on nerves must have been of rare occurrence, so that in the great majority of the clinical cases under examination it was impossible to determine the exact form and degree of injury which the nerves had suffered.

Again, it would seem that a large number of the cases studied were those of paralysis of the seventh nerve of the so-called "rheumatic" type. Under ordinary conditions of life this is of all peripheral nerves the one most often affected. Moreover, it is one which on account of its position, and the position of the muscles which it supplies, is most easily studied. Next in frequency to the facial muscles come the intrinsic muscles of the hand. Of the four cases which Erb describes in his original communication, three are cases of Bell's palsy, while the fourth is an injury to the ulnar nerve. As we shall see later, both the facial muscles and the small muscles of the hand and foot are peculiar in their behaviour.

CHAPTER II.—POLARITY OF NORMAL AND DEGENERATED MUSCLE.

(1) *Unipolar Stimulation.*

The infallibility of polar reversal as an absolute sign of degeneration has recently been challenged by many observers. At the present day, in fact, some neurologists discredit it altogether. With a view to determining whether polar reversal occurs, and, if so, what is the true significance of the phenomenon, I have subjected some hundreds of cases of nerve injury to the test. The first method I employed is that which is commonly followed. One electrode (called the testing electrode) is placed on the muscle near its proximal end. The other (the so-called indifferent electrode) on some distant part proximal to the muscle. Make and break are effected automatically by means of a metronome, thus obviating any source of error due to movement of the testing electrode. The kathode having been placed upon the muscle the current was increased by a rheostat until a minimal contraction appeared. The electrode was then moved about until the most excitable part of the muscle was discovered. The amount of current in milliamperes which caused a minimal contraction at this point was read off by an assistant. The current was then reversed, and the minimal exciting current at the same point determined. The corresponding muscle of the opposite side was then tested in the same way. The results are given in Tables I, II and III.

If we first consider Tables I and II, which are taken from cases of injury of the musculospiral and sciatic nerves, we find that excluding Case I, which was examined only nineteen days after injury, with K.C.C. a stronger current was required to evoke contraction on the degenerated side than on the normal side. In the case of A.C.C. the relative excitability on the two sides is variable. Further on the normal side K.C.C. is invariably more effective than A.C.C., while on the degenerated side we have $K.C.C. = A.C.C.$, $K.C.C. > A.C.C.$ or $A.C.C. > K.C.C.$ In the fourth and eighth columns I express the difference as a fraction of the total current. It will be noticed that in the great majority of cases the difference between K.C.C. and A.C.C. is, relatively to the strength of current used, much greater on the normal than on the degenerated side. The small differences are within the bounds of experimental error in the case of paralysed muscles, so that one may say that as a general rule degenerated muscle is indifferent to the polarity of the electrode. Lastly, there is no relationship between the

TABLE I.—MUSCULOSPIRAL PARALYSIS.

Case No.	Regimental No.	Period after injury	Condition of nerve	Muscle	PARALYSED SIDE				NORMAL SIDE			
					K.C.C.	A.C.C.	Diff.	Diff. K.C.C.	K.C.C.	A.C.C.	Diff.	Diff. K.C.C.
1	2696	19 days	Completely divided ..	Ext. com. digit; ext. oss. met. poll.	{ 5.0	7.0	+ 2.0	0.4	7.0	9.0	+ 2.0	0.29
2	10329	39 "	" "	Ext. com. digit	{ 5.0	5.0	2.5	4.0	+ 1.5	0.6
3	—	3 months	" "	Ext. com. digit; ext. oss. met. poll.	{ 3.7	3.6	- 0.1	0.03	3.5	4.3	+ 0.8	0.23
4	2565	3 "	" "	Ext. com. digit; ext. oss. met. poll.	{ 5.0	5.0	3.0	5.0	+ 2.0	0.66
5	13031	4 "	" "	Ext. com. digit; ext. oss. met. poll.	{ 4.0	4.0	2.0	3.0	+ 1.0	0.5
6	15808	52 days	Inflamed and adherent	Ext. com. digit	{ 11.0	11.0	+ 2.0	0.2	5.0	6.5	+ 1.5	1.0
7	1726	45 "	Involved in scar tissue	Ext. com. digit; ext. carp. rad. long.	{ 10.0	12.0	+ 2.0	0.2	3.0	6.0	+ 3.0	..
8	4361	38 "	" "	Ext. com. digit	{ 5.0	6.0	+ 1.0	0.2	0.66
9	8044	36 "	Severely damaged " by scar tissue	Ext. com. digit; ext. indicis..	{ 13.5	16.0	+ 2.5	0.19	5.1	8.5	+ 3.4	0.4
10	16289	36 "	" "	Ext. com. digit	{ 12.0	12.5	.. 0.5	0.04	2.5	3.5	+ 1.0	0.66
11	13036	40 "	Not examined surgically	Ext. com. digit; ext. oss. met. poll.	{ 4.5	4.5	3.0	5.0	+ 2.0	..
12	24998	2 months	" "	Ext. com. digit; ext. oss. met. poll.	{ 7.0	7.0	0.25
13	1606	3 "	" "	Ext. com. digit; ext. oss. met. poll.	{ 6.0	6.0	4.0	5.0	+ 1.0	0.1
14	11512	7 weeks	" "	Ext. com. digit; ext. supin. longus	{ 7.0	7.0	2.0	4.0	+ 2.0	0.1
					{ 5.0	4.0	- 1.0	0.2	2.6	3.1	+ 0.5	0.19
					{ 5.0	6.0	+ 1.0	0.2	2.5	3.5	+ 1.0	0.4
					{ 1.5	2.2	+ 0.7	0.47	{ 1.2	1.5	+ 0.3	0.25
					{ 2.2	2.4	+ 0.2	0.1	1.0	1.6	+ 0.6	0.6
					{ 10.0	12.5	+ 2.5	0.25	1.5	2.0	+ 0.5	0.33
					{ 9.8	10.2	+ 0.4	0.04	7.0	8.0	+ 1.0	0.14
					{ 9.0	9.0	..	0.1	8.0	11.0	+ 3.0	0.37
					{ 10.0	9.0	- 1.0	0.1	2.0	3.8	+ 1.8	0.9
					{ 11.0	11.0	1.5	3.3	+ 1.8	1.2
					{ 11.0	11.0	0.3	2.3	+ 2.0	6.6

TABLE II.—PARALYSIS OF GREAT SCIATIC NERVE.

Case No.	Regimental No.	Period after injury	Condition of nerve	Muscle	PARALYSED SIDE				NORMAL SIDE			
					K.C.C.	A.C.C.	Diff.	Diff. K.C.C.	K.C.C.	A.C.C.	Diff.	Diff. K.C.C.
15	3023	59 days	Complete division ..	Tibial. ant. .. Gastrocn. ..	9.5 13.0	10.5 17.0	+ 0.5 + 4.0	0.05 0.31	5.0 7.0	11.0 17.0	+ 0.60 + 10.0	1.20 1.40
16	—	8 months	Involved in scar ; very slight return of voluntary power	Peron. long. .. Tibial. ant. ..	21.0 12.0	18.0 12.5	- 3.0 + 0.5	0.14 0.04	8.0	17.0	+ 9.0	1.125
17	851	24 days	Not examined surgically	" "	8.0	10.0	+ 2.0	0.25	3.0	7.0	+ 4.0	1.33
18	44954	14 weeks	Complete division ..	" "	20.0	24.0	+ 4.0	0.20	3.0	9.0	+ 6.0	2.0
19	1338	11 months	Involved in scar tissue	" "	5.0 4.5	5.5 4.5	+ 0.5 0	0.10 0	2.0 8.0	5.0 12.0	+ 3.0 + 4.0	1.50 0.50

TABLE III.—PARALYSIS OF MEDIAN AND ULNAR NERVES.

Case No.	Condition of nerve	Muscle	PARALYSED SIDE				NORMAL SIDE			
			K.C.C.	A.C.C.	Diff.	Diff. K.C.C.	K.C.C.	A.C.C.	Diff.	Diff. K.C.C.
21	Median and ulnar severely damaged	Abduct. poll.	1.8	1.9	+ 0.1	0.05	0.8	0.8
22	Resection and suture Median : involved in scar tissue	Dorsal interossei Abduct. poll.	3.7 2.3	5.1 2.3	+ 1.4 ..	0.33 ..	2.4 ..	2.2 ..	- 0.2 ..	0.08 ..
23	Median : complete division	" "	4.5	4.1	- 0.4	0.09	3.0	3.3	+ 0.8	0.27
24	Median : involved in scar tissue	Oppon. poll.	9.5	5.0	- 4.0	0.42	3.0	4.1	+ 1.3	0.43
25	Ulnar : involved in scar tissue	Dorsal inteross.	8.0	10.0	+ 2.0	0.25	6.0	10.0	+ 4.0	0.66
26	Ulnar : no operation	" "	6.0	8.0	+ 2.0	0.33	7.0	6.0	- 1.0	0.14
27	" "	" "	10.0	6.5	+ 3.5	0.35	5.0	5.0

NOTES TO TABLES I, II, AND III.

(1) The figures indicate the current in milliampères required to produce minimum contraction.

(2) In the fourth and eighth columns of figures I have represented the difference as a fraction of the total current (K.C.C.).

(3) In the third and sixth columns of figures a + sign indicates K.C.C. > A.C.C. : a - sign indicates A.C.C. > K.C.C.

(4) In the cases where the nerve was not examined surgically, evidence of severe injury was indicated by the absence of response to Faradism and the sluggish response to the constant current.

polarity of the muscle and the degree of injury which the nerve has sustained.

Table III shows the results obtained from cases of injury to the median and ulnar nerves. It will be observed that all the muscles examined are the intrinsic muscles of the hand. Again we see the variable K.C.C. : A.C.C. relationship obtaining in the degenerated condition, but in these cases we find the same variability on the normal side, reversal of polarity occurring with approximately equal frequency on the two sides.

(2.)

In stimulating the motor point of a normal muscle we are dealing with a nerve-muscle complex, the current affecting three different "receptive substances." There are the intramuscular branches of the nerve, and there is the muscle tissue proper. In addition, Langley [15] has shown that there exists in between yet a third distinct substance, existing as a kind of synapse between nerve and muscle. This has been confirmed by Keith Lucas [18], who finds that these three receptive substances can be distinguished by their excitability. The least excitable (Lucas's α substance) being the muscle proper, and therefore present equally in all parts of the muscle, the most highly excitable (β) being the substance at the synapse or neuro-muscular junction, while the purely nervous substance (γ) is intermediate in excitability. With one electrode placed over the motor point of the muscle the three substances will be affected to a varying extent depending upon their excitability. The β substance will therefore preponderate, and we must regard the mechanical effect as the result mainly of stimulation of this substance.

Now, there is one point which must be mentioned here, since it is too often forgotten in clinical work, and that is the difference between the real and the apparent electrodes. Supposing we place the negative electrode on the motor point of the biceps and the positive electrode on the side of the neck. On closing the circuit the current flows into the body at the neck and leaves it at the arm. But it would be absurd to say that the kathode is at the muscle and the anode on the neck. The true anode is the point or points at which the current enters the muscle, and the true kathode is the point or points at which it leaves the muscle. As the current leaves the positive electrode at the neck it spreads out diffusely according to the resistance offered by the tissues, it enters the muscle diffusely, and in the case before us where the

muscle is large and superficially placed, it leaves the muscle concentrated at the point nearest to the negative electrode. This is shown diagrammatically in figs. 1 and 2. The negative field is the more concentrated, and will exert a greater physiological effect than the more diffuse positive upon the neuro-muscular substance, since this is in the immediate neighbourhood of the former. On reversing the current we get the opposite state of affairs. The current enters the muscle (anode)

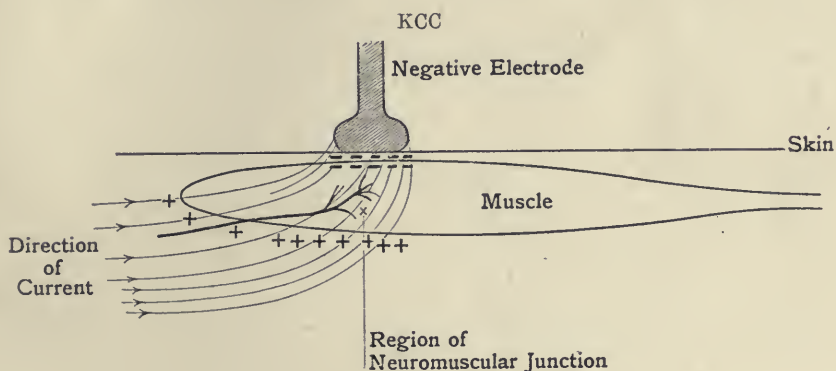


FIG. 1.

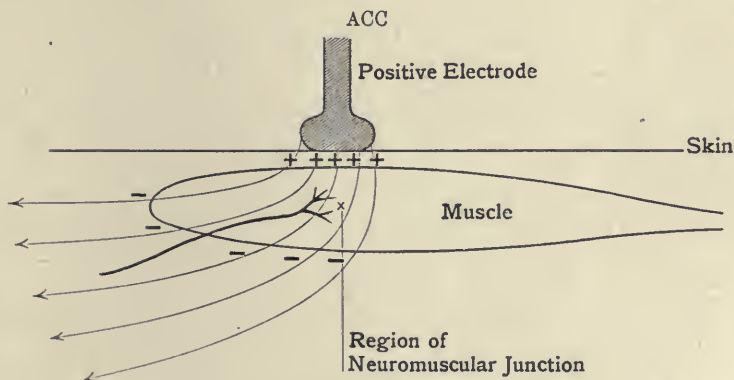


FIG. 2.

concentrated in the region of substance β , leaves it diffusely (kathode), the anode therefore exerting the greater effect. Now if we test the polarity of a normal muscle at different points on its surface we find that the normal condition $K.C.C. > A.C.C.$ is obtained with constancy only at the motor point. At other parts of the muscle the relationship is variable. This is shown in Table IV.

TABLE IV.—EFFECT OF VARYING POSITION OF ELECTRODE.

Case (28) of Complete Division of Sciatic Nerve. Muscle—Tibialis anticus. The figures indicate amount of current required to produce minimal contraction.

Position of testing electrode	PARALYSED LIMB		NORMAL LIMB	
	K.C.C.	A.C.C.	K.C.C.	A.C.C.
Proximal end of muscle	15	15	1.5	5.0
Middle of muscle	15	15	4.0	6.0
Distal end of muscle	11	14	10.0	9.0

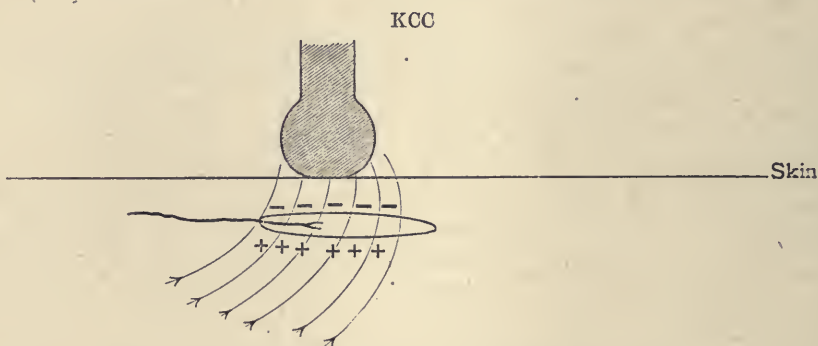


FIG. 3.—True anode and kathode in the case of a short muscle.

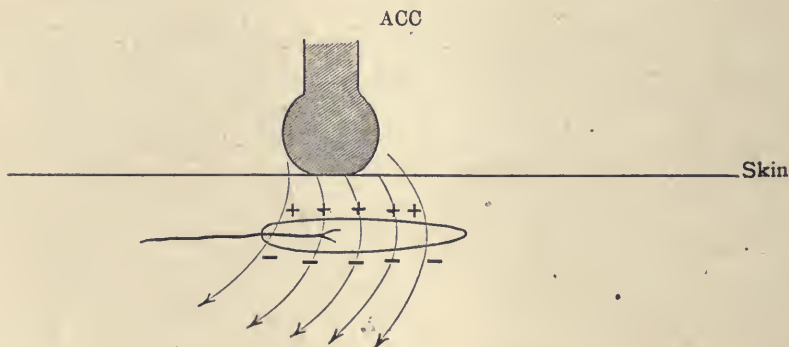


FIG. 4.

When degeneration occurs the *first* change is the disappearance, as we shall see later, of the physiological "motor point"—all parts of the muscle becoming equally excitable. From these facts one may conclude that the indifference to polarity which we have seen is characteristic of the degenerated condition, is due to the absence of the

neural and neuro-muscular substances, the muscle proper responding directly to the stimulus.

It now remains to explain the anomalous behaviour of the normal muscles in Table III. All the muscles here are of very small size compared with those of Tables I and II. In testing these small muscles it is a matter of much greater difficulty to single out the motor point and to obtain a concentrated effect at the point of entry or of exit. The current enters the muscle diffusely and leaves it diffusely. Consequently we cannot tell whether the muscle is being stimulated at the point of entry or at the point of exit of the current. This is shown in figures 3 and 4.

It is sometimes stated that in testing the intrinsic muscles of the hand the so-called indifferent electrodes should be placed on the opposite side of the hand in testing the dorsal interossei, for instance, the indifferent electrode should rest against the palm of the hand. This practice I believe only aggravates the anomalous behaviour of these muscles, since the current is thus being made to pass at right angles to the direction of the muscle fibres. I have obtained more consistent results by placing the indifferent electrode on the arm.

(3) *The Longitudinal Reaction.*

It has long been known that in a normal muscle contraction is most easily evoked at the motor point while in degenerated muscle, it can often be activated more easily at the distal end. This was called the Longitudinal Reaction. This, as Lewis Jones [12] pointed out, was due to the destruction of the neural elements, leaving the muscle equally excitable at all points of the surface. This effect is, however, obtained only when the indifferent electrode is placed on some part of the body proximal to the muscle, and this for a very simple reason. When the testing electrode is placed distally the muscle is brought under the influence of the current as shown in figures 5 and 6. Consequently as all parts of the muscle are equally excitable the physiological effect will be greater. But in the normal muscle the motor points being much more irritable than any other part of the muscle, this effect is not seen.

(4) *Effect of Increasing the Stimulus upon Polarity.*

If instead of taking minimal contractions as our guide, we study the changes in the K.C.C.: A.C.C. relationship a further remarkable

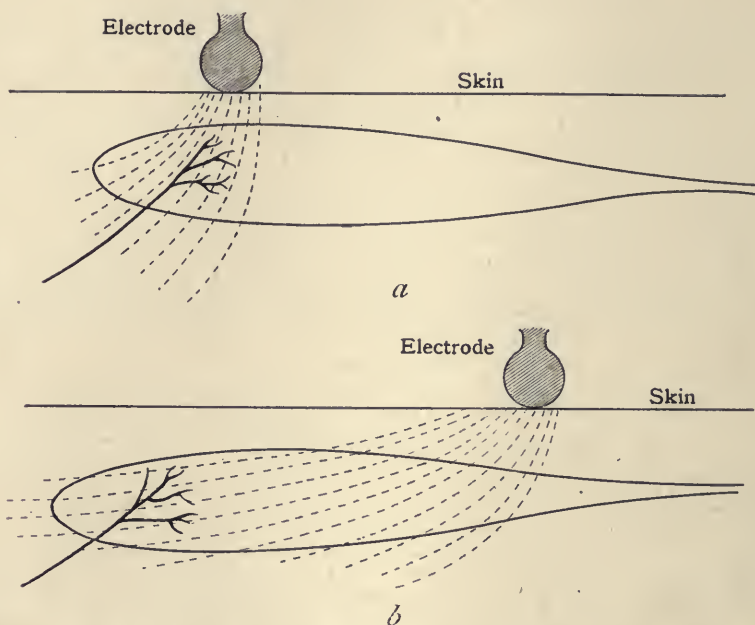


FIG. 5.—Illustrating the longitudinal reaction. In the normal muscle *a* is more effective than *b*, owing to the condensation of field at the motor-point in the former.

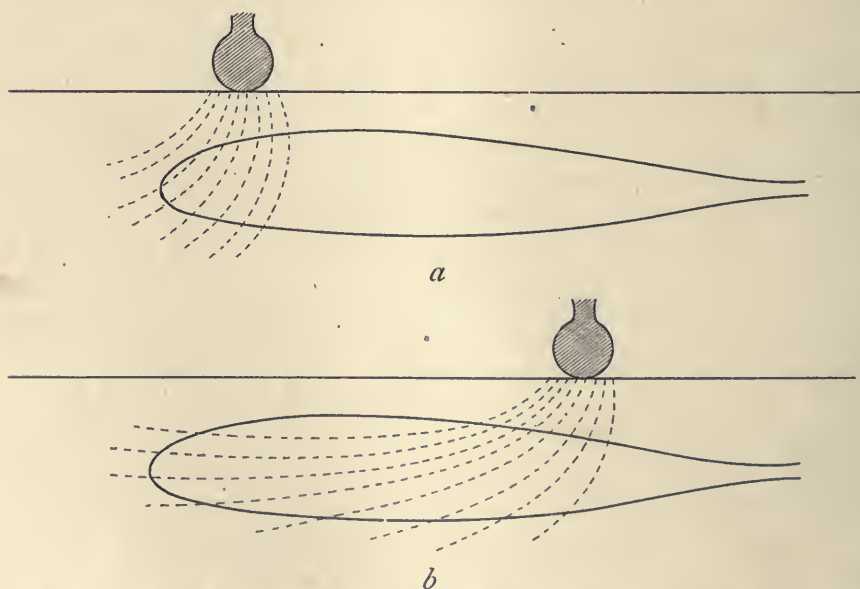


FIG. 6.—Illustrating the longitudinal reaction in the degenerated muscle. The muscle being equally excitable all over, owing to the absence of the "motor-point," *b* is more effective than *a*, since in the former more of the current traverses the muscle.

difference in the behaviour of normal and degenerated muscle is seen. Taking the healthy muscle first we find the amount of current required to give minimal contractions with K.C.C. and A.C.C. With the kathode on the muscle we then increase the current until a full contraction is obtained. This having been recorded, the current is then reversed, and the current required to evoke an equal contraction is determined. The degenerated muscle is then tested in the same way.

TABLE V.—EFFECT OF INCREASE OF STIMULUS ON K.C.C. : A.C.C. RELATIONSHIP.
MUSCLE—TIBIALIS ANTICUS.

Case No.	Case	Limb	MINIMAL CONTRACTION			FULL CONTRACTION		
			K.C.C.	A.C.C.	Diff.	K.C.C.	A.C.C.	Diff.
29	Pte. McC.	Normal limb	5	11	6	14	25+	9+
		Degenerated limb ..	Stimulation painful					
30	Pte. W.	Normal limb	2	5	3	7	13	6
		Degenerated limb ..	15	20	5	35	37	2
31	2nd Lieut. S.	Normal limb	5	8	3	10	17	7
		Degenerated limb ..	17	17	0	—	—	—
32	Pte. McD.	Normal limb	5	11	6	13	22	9
		Degenerated limb ..	10	12	2	20	20	0
33	—	Normal limb	3	9	6	4	12	8
		Degenerated limb ..	20	24	4	—	—	—

Table V gives the result of the examination of five cases in this way. It will be noticed that in the case of the normal muscle, as the strength of contraction increases, the difference between K.C.C. and A.C.C. also increases. In the degenerated state, on the other hand, increasing the force of the contraction does not materially affect the polarity—the difference being small in any case.

(5) Bipolar Stimulation.

A muscle can also be stimulated by placing both electrodes over it, one at either end. I have tested this method and find that the results obtained are almost exactly the same as are obtained by the unipolar method. With the kathode at the proximal end and the anode at the distal end the current is descending the muscle and vice versa. Owing to the propinquity of the motor point to the proximal end we have in normal muscle—

Descending > Ascending.

In the case of degenerated muscle, the relationship is variable, but any difference is comparatively slight.

Summary of Chapter II.

(1) In the case of long muscles in the normal condition we find $K.C.C. > A.C.C.$ This is constant.

(2) In degeneration the muscle is almost indifferent to polarity. This is due to the disintegration of the neural and neuro-muscular elements at the motor point.

(3) The normal $K.C.C. > A.C.C.$ is only obtained with constancy when the testing electrode is placed over the motor point.

(4) In normal short muscles such as those of the hand or face, the difficulty of singling out the motor point is responsible for the inconstancy of the results obtained.

(5) The "longitudinal reaction" as usually tested is due to the greater amount of current traversing the muscle when the testing electrode is distal than when it is proximal.

(6) In normal muscle the $K.C.C. : A.C.C.$ difference increases with increase of stimulus. In degenerated muscle the response is indifferent whatever the strength of current.

(7) The "bipolar" has no advantage over the "unipolar" method.

CHAPTER III.—FURTHER OBSERVATIONS ON DEGENERATED MUSCLE.

(1) Increased Galvanic Response.

We have seen that the quantitative change in the response to the constant current was the subject of dispute between Erb and Vulpian. Erb asserted the invariable increase in galvanic excitability, beginning in the second week and lasting as long sometimes as two months. But he afterwards modified this statement, admitting that in some cases of paralysis of the lower limbs the phenomenon did not appear. Experimenting upon rabbits in which the bare muscle is stimulated, I have found this to be a constant sign; about three weeks after nerve section, the increased response to the galvanic current with the diminished response to the faradic current is indeed very striking. In clinical work on the other hand the results obtained are less constant. A stage of increased excitability to the constant current can sometimes be recognised, but not always. The fact is I believe theoretically such a stage always occurs. I have already called attention to the imperfections of apparatus used in Erb's time. Even with all the improvements of the present day we still have no means of estimating the strength of current which is actually stimulating the muscle as

distinguished from the strength of current which is passed into the body.

Owing to the impossibility of making stimuli which are physiologically equal on the two sides of the body, no true quantitative estimate of excitability can be made. I regard then the increased galvanic response as a constant and necessary part of the reaction of degeneration in an early stage, but one which cannot always be demonstrated owing to imperfections of technique. At the same time it is possible that the phenomenon is not so well developed in human muscles as in those of the rabbit.

(2) *Absence of Response to the Constant Current.*

Degenerated muscle may respond to the constant current for a very long time. Sherren [27] quotes a case of complete division of the musculo-spiral nerve in which the muscles responded twenty-three years after the injury. It would appear that a response is obtained as long as any contractile material remains, that is to say until the muscle has completely atrophied, or has been replaced by fibrous tissue. As however there are certain conditions under which the constant current fails to evoke any contraction, these must be described.

The average adult patient can usually tolerate the galvanic current of strength sufficient to cause contraction of the muscle. In some cases of course owing to temperamental conditions or, in cases of incomplete injury to referred pain, caused by the irritation of the nerve trunk it becomes difficult to bring the required strength of current into play. There are too, certain regions of skin where the electric current is particularly unpleasant. I have found the front of the thigh to be of this nature, making the examination of the quadriceps extensor and sartorius often very difficult.

The presence of œdema has a very marked effect upon the response. A small excess of fluid in the subcutaneous tissue at the point of application of the electrode is sufficient to prevent the contraction even of normal muscle to either form of current. The reason for this no doubt is that the subcutaneous fluid is a better conductor than the muscle. The current flows along the line of least resistance without touching the deeper structures.

Failure to respond to the constant current also occurs when the muscle itself is damaged. This is a point of some diagnostic importance. Recently a patient was brought to me suffering from a gunshot wound

of the forearm. All the muscles responded normally except the flexor longus pollicis which gave no reaction whatever. In this case the muscle itself was damaged, since had the typical "reaction of degeneration" been obtained it would have signified injury to the branch which the median nerve supplies to this muscle.

(3) *Return of Faradic Excitability.*

As we have seen in our historical survey, it was taught in the seventies that voluntary power returns before the response to the faradic current. Some recent observers, however, have found that this is usually but not always the case. In my own experience voluntary power returns first in normal cases. Usually the muscle attains to considerable strength before it responds to the interrupted current. Cases in which response to faradism occurs while still completely paralysed come into two categories. There are those where the patient has never been encouraged to exert his will power and has never even tried to use the muscles. In other cases there is a "functional" element superadded to the organic mischief. These cases never fail to respond to encouragement and other appropriate measures.

Summary of Chapter III.

(1) Increased galvanic excitability is a necessary stage in the process of degeneration. It cannot however always be recognized. It may be less evident in man than in the rabbit.

(2) Absence of galvanic response occurs: (1) in cases of very long standing; (2) as a result of hypersensitiveness of the skin; (3) when œdema is present; (4) when the muscle itself is injured.

(3) In regeneration, voluntary power returns before faradic excitability, except in functional cases and those in which the extent of voluntary power is not realized by the patient.

CHAPTER IV.—CONDENSER DISCHARGES.

In the early days of electromyology it was known that degenerated muscle failed to respond to the faradic current because the individual impulses were of so short duration. Many attempts have since been made to stimulate muscles by known quantities of electricity, and so to estimate different grades of degeneration according to the minimum duration of current to which the muscle responds. For this

purpose condensers were introduced, first by Boudet in 1888; their use was afterwards extended by Dubois [7]. In this country the chief exponent of this system of testing was Lewis Jones, who introduced a set of twelve condensers, the capacity and discharge duration of which, at a voltage of 100, are these:—

Capacity in microfarads				Duration of discharge
0.016	$\frac{1}{24000}$ sec.
0.025	$\frac{1}{16000}$ "
0.05	$\frac{1}{8000}$ "
0.62	$\frac{1}{6000}$ "
0.08	$\frac{1}{4800}$ "
0.125	$\frac{1}{3200}$ "
0.25	$\frac{1}{1600}$ "
0.33	$\frac{1}{1400}$ "
0.5	$\frac{1}{800}$ "
0.66	$\frac{1}{600}$ "
1.0	$\frac{1}{400}$ "
2.0	$\frac{1}{200}$ "

A further modification has recently been introduced by Hernaman-Johnson [11], by which the voltage can be varied. It is supposed that, by finding the smallest charge which will cause stimulation, an absolute value can be given to the stage to which degeneration has advanced and that day to day tests give a measure of the progress of the case.

Let us now consider whether the condenser gives that exact scientific information which it is alleged to give and whether we can obtain by its means any information of value which cannot be got by means of the faradic and galvanic currents.

Of the constant nature of the capacity of a given condenser there can of course be no question. But before we can consider the condenser as an instrument of exact scientific measurement we must have some means of finding what proportion of the charge passes through the muscle and stimulates it. To say that in the ordinary process of stimulation the whole charge is effective is absurd. The muscle responds to that part of the charge which passes through it, not to the whole charge which passes through the body. At present we have no means of estimating the amount of the part which is active. Comparison with the corresponding muscle of the healthy limb, although some sort of guide is open to the same fallacy as in the case of the constant current—that is to say, the varying conditions on the two sides—the size of the muscle, the state of the subcutaneous tissue. Further, if the result obtained at one examination of the muscle cannot be regarded as a definite standard, it follows that the results obtained

from a series of examinations at intervals of some weeks or months will have still less value. Besides the condition of the muscle many other factors will be different on the two occasions—the position of the electrodes, the amount of subcutaneous fat and the temperature of the skin, in spite of (or in consequence of) artificial attempts at keeping the skin warm. With so many varying factors the amount of electrical energy which is available for the stimulation of the muscles must be subject to very considerable variation. So far from being more scientific than the constant current method, it is in reality less so, for by estimating the relative excitability to K.C.C. and A.C.C. we have only one variant—the direction of the current. We are here comparing the effect of a given current with that of the same current reversed, all other factors being unaltered.

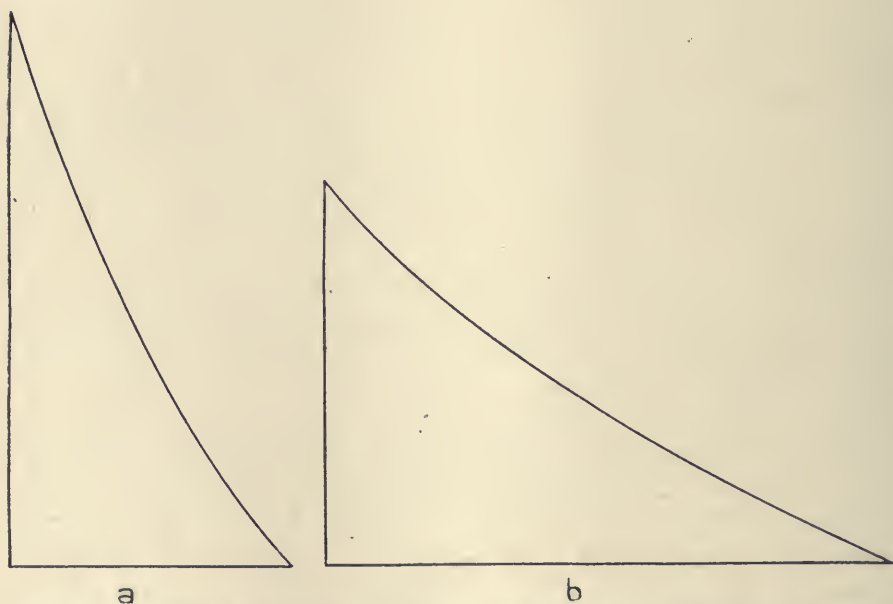


FIG. 7.—Discharge of condenser: *a*, through low resistance; *b*, through high resistance.

Those who advocate the use of the condenser lay great stress on the fact that with increase of the capacity of the condenser, voltage being constant, there occurs a proportional increase in the duration of the discharge. But the discharge duration, so far from being constant, varies with the external resistance of the circuit.

Figs. 7 *a* and *b* show the difference in the form of discharge with small and with high resistance. It is idle to suppose, as has been

supposed by some, that the resistance of the body is a negligible quantity. A short experience of passing current through the body will be sufficient to convince anyone that the resistance offered by the body is considerable, quite sufficient at any rate to alter the duration of discharge. But even if the duration were independent of any external circumstance it is difficult to see what scientific value can be attached to its expression. We have already seen that the stimulating effect of the constant current depends upon two factors, strength (voltage) and duration, which are related inversely. Further, there is a threshold voltage below which contraction does not occur even with infinite duration. Consider the discharge A—B. The current falls rapidly to

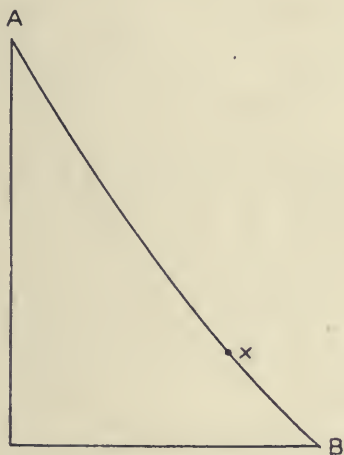


FIG. 8.

zero at B. At a certain point x it reaches the minimum effective voltage. The part xB of the current is therefore totally without physiological effect, and since we have no means of knowing the exact position of the point x we cannot tell the duration of the effective current. Moreover, as the inclination of the curve varies with resistance so the distance of x from A and B will vary, a fact which further complicates the question.

Another factor which must be taken into account is the direction of the current in relation to the direction of the muscle fibres. Leicher [17] showed that with a given current the maximum effect is produced when the current traverses the muscle longitudinally. If the current passes absolutely at right angles to the direction of the fibre it is

without effect. The position of the electrodes, therefore, is all important if accuracy is the objective. In the method adopted by some, namely, pinching up the muscle between the electrodes, the electrical discharge is acting at the greatest physiological disadvantage.

It must be admitted, however, that the condenser discharge possesses one great advantage over the galvanic current in that it is comparatively painless, but as a set-off against this must be stated the undoubted fact that the condenser discharge spreads more diffusely in its passage between the electrodes, and consequently it is more difficult to limit the effect to one muscle.

A more scientific method was introduced in 1903 by Leduc, who invented a means of interrupting the constant current mechanically in such a way that the duration of current as well as the interval between could be altered. Both were capable of measurement. But the apparatus was so complicated that the method never came into general use in this country.

Even if the condenser did give an absolute value it is doubtful if the results would be of any constant practical use as a test of recovery. We have seen that usually voluntary power returns before the faradic response. If the testing is performed by means of the condenser it will be found that voluntary power will usually have begun to return before there is any change in the electrical response. Here then the condenser possesses no advantage over the constant current.

In conclusion, we may say then that the condenser does not give the accurate estimate of degeneration which is attributed to it. It is indeed no royal road to diagnosis and prognosis. It may in some cases be of use in supplementing the information obtained from the older methods, but these on the whole are preferable. The animal body is from an electrical point of view terra incognita, the mysteries of which are not to be explored by the further elaboration of apparatus in the direction of obtaining graded stimuli, the accuracy of which is upset by a varying and unknown resistance.

Summary of Chapter IV.

(1) The defects of the condenser are that the discharges vary with the resistance and with other factors. They do not give uniform results either in theory or in practice. It is difficult to confine the discharge to any individual muscle.

(2) The one advantage of condenser discharge is that they do not cause pain.

CHAPTER V.—THE NATURE OF THE DEGENERATIVE CHANGES.

When we come to consider the changes following section of a motor nerve we are forced to admit that in the past investigation has been directed far more towards the changes occurring in nerve than towards those occurring in muscle. The controversy upon the regeneration of nerve has been partly responsible for this. But the process of degeneration does not stop short at the nerve-ending, the regressive changes in muscle are something more than disuse atrophy following paralysis of the nerve. Clearly, the disintegration of the nerve-endings within the muscle, although it may affect the degree of response of the muscle to artificial stimuli, cannot by itself explain the striking change in the form of the contraction. This must be due to some change in the muscle itself.

The muscle-fibre no less than the nerve-fibre is dependent upon its connection with a healthy anterior cornual cell for the maintenance of its normal structure and excitability. This is not surprising when we remember that in the earliest metazoa contractile tissue first appears in the form of fibrils laid down in a cell another part of which is adapted to the reception of stimuli, the whole cell being dependent functionally upon the nucleus. The same cell is receptor, conductor and effector, to use Sherrington's nomenclature. In higher forms, in spite of the increasing complexity of the reflex arc, the central part of the mechanism exerts upon the effector organ an influence which involves more than the mere discharge of impulses. The anterior cornual cell is still the trophic centre of the muscle-fibre as well as of the nerve-fibre. Judged from this point of view the muscle is merely a special modification of one end of the conductor mechanism as the receptor organ is at the other.

We shall now proceed to consider why, after section of a nerve, the brisk normal twitch gives place to the sluggish response characteristic of degeneration.

(1) *The Process of Degeneration in White and Red Muscles of the Rabbit.*

In striped muscle, fibres of two kinds are found, the white and the red. These are distinguished from one another histologically and physiologically. In structure the red fibres have a greater amount of sarcoplasm than the white, and have also a certain peculiar arrangement of blood-vessels first pointed out by Ranvier [23], the significance

of which is not known. On stimulation white fibres respond briskly while the red fibres respond with a sluggish contraction after a comparatively long latent period. In man each individual muscle is composed of a mixture of both kinds of fibres, while in some animals, notably the rabbit, different muscles are composed exclusively of one kind or the other, the gastrocnemius for instance being purely white, and the soleus purely red.

Now the contraction of normal red muscle bears at first sight a resemblance to that which is obtained from degenerated human muscle. It might be thought, therefore, that the reaction of degeneration as found in man is due to the process of degeneration affecting the white and red fibres at unequal rates, the former degenerating more rapidly than the latter, so that at a certain stage in the process the red fibres alone respond to electrical stimulation. In other words, the reaction of degeneration is brought about by the unmasking of the red fibres owing to the rapid death of the white kind.

But that this hypothesis of degeneration is improbable is shown by the following considerations:—

(1) The resemblance between the mixed degenerated muscle of man and the pure red muscle of the rabbit is more apparent than real. In the degenerated condition response to induction shocks is very difficult to obtain, even though at the same time the excitability to the constant current may be considerably exalted. In the normal soleus of the rabbit the single induction shock is just as efficient a stimulus as the constant current. Moreover, this is still the case after the administration of curare, showing that stimuli of momentary duration affect this type of muscle directly and not through the nerve endings.

(2) This hypothesis presupposes the more rapid degeneration in the white fibres than in the red. It has been stated by Joteyko that such is the case, but after a careful examination of several rabbits I am unable to find any foundation for this statement. If there is any difference in the behaviour of the two varieties of fibre it would appear in the opposite direction. According to my results the red muscles degenerate in the majority of cases more rapidly than the white. If we take loss of weight as an indication of the rate of degeneration the results shown in Table VI (p. 342) indicate that there is no constant difference in the amount of wasting shown by the gastrocnemius and soleus. I admit, however, that this is a poor criterion, since atrophy is no doubt partly due to disuse.

(3) The degenerative process in the pure white muscle corresponds fairly closely to the process as it affects the mixed muscle of the human being. It would appear, therefore, that in the latter it is always the white fibres which respond whatever may be the stage of degeneration. Normally the white fibres being more excitable, and responding more briskly than the red, determine the rate of contraction of the whole muscle. The process of degeneration would, therefore, seem to be due to changes occurring in white fibres mainly.

(4) The "reaction of degeneration" is a change which occurs not slowly as may be supposed from its name, but with comparative suddenness, as has recently been shown by Paton and Findley [22]. It is difficult to explain this by assuming that the white fibres become suddenly inexcitable some few days after section of the nerve.

Although we cannot in this way explain the phenomena of degeneration as they occur in man, the comparative study of the electrical behaviour of the two varieties of muscle fibre does throw some light on the problem before us.

I have followed the process of degeneration in the muscles of the rabbit's hind leg after resection of a portion of the sciatic nerve in the thigh. Rabbits were examined at different periods ranging between four days and four months after neurectomy. In all cases the left nerve was cut, the right side being used as a control. In each case before the muscles were investigated the condition of the nerve was examined to ensure that the operation of neurectomy had been effective. The muscles were stimulated by means of small sponge electrodes, soaked in salt solution, which were laid on the bare muscle. Where it was desired to take tracings the tendon was cut, the muscle freed from the surrounding tissues, except at its proximal attachment, and the distal end was attached to the recording lever.

(2) *Electrical Behaviour of White Muscle.*

The excitability to the interrupted current diminishes rapidly, but does not disappear until many weeks have elapsed. As long as three months after section of the nerve a slight contraction can be obtained, using very strong currents. It is difficult, however, as late as this to produce a contraction of the muscle; as a rule, all that occurs being, as Erb pointed out, a contraction of the fibres adjacent to the electrodes. Experimentally, therefore, faradic response is not an absolute test of degeneration, though clinically it is so owing to the limitations of stimulation due to the resistance of the skin and human powers of

endurance. Erb mentions a case where, in spite of an injury to the nerve, faradic response was present. I have never come across such a case and am very doubtful whether it can occur after complete division, sufficient time of course having elapsed to allow of degeneration.

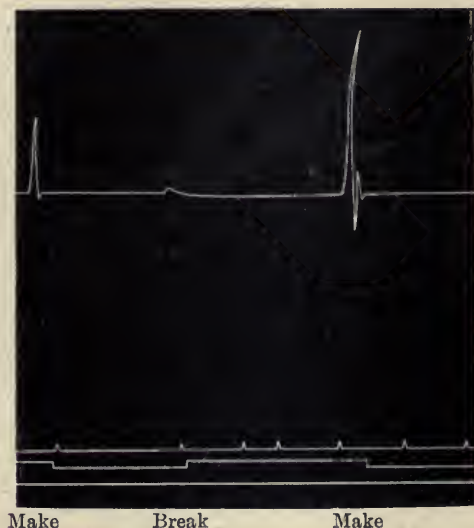


FIG. 9. -Tibialis anticus. Eight days after section of nerve. Tonus has not yet appeared.

The excitability to the constant current is unaltered as far usually as the eighth day (fig. 9), a brisk twitch occurring at make, and if the current be not too weak, at break, the muscle remains uncontracted while the current is passing. During the second week two well-marked changes occur. The first is the increased excitability to this form of current, coincident, it must be remembered, with a diminished response to the faradic current. At the same time the phenomenon of galvanotonus appears—the muscle remains contracted while the current is passing. This was first demonstrated by Fick [10] for degenerated amphibian muscle.

(3) *Characteristics of Galvanotonus.*

Fig. 10 shows the condition found in the gastrocnemius fourteen days after section of the nerve. With a weak stimulus (fig. 10, I) the contraction both at make and at break is of a double nature, the first being a twitch just as brisk as the response of the normal muscle, the second a slower contraction which appears after the first. In the

tracing this appears first as the arrest of the relaxation following the twitch. On increasing the current the slower contraction becomes further developed until it forms a tonic contraction which persists during the passage of the current. At break there is again a twitch before relaxation, the lever rising as it were above the plateau of the persistent contraction.

The question now arises whether the second element in the contraction is due to the rapid change of potential as in the case of the primary twitch or whether it is due to the persistence of the current.

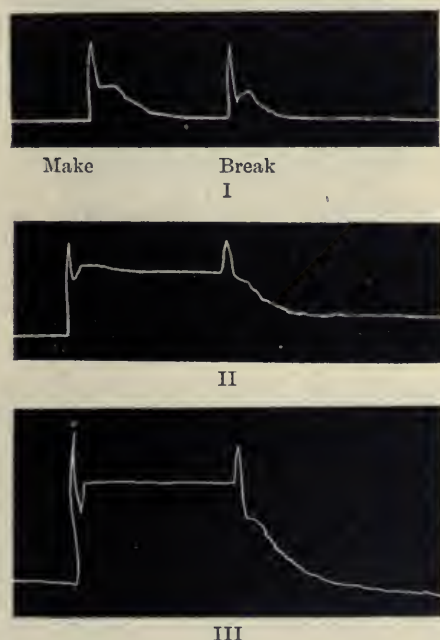


FIG. 10.—Rabbit's gastrocnemius fourteen days after section of sciatic nerve, showing effect of increasing the stimulus.

A glance at fig. 10 I shows that the contraction at break is of a double nature just as the contraction at make. Rapid change of potential is therefore the cause of the second part of the contraction as well as of the first.

If the degenerated muscle is stimulated with a weak single induction shock, the result is a simple twitch (fig. 11 *a*). With stronger shocks the second element appears, but is not well marked (fig. 12). This shows that with currents of momentary duration the main effect is

twitch, the second element being less prominent than when currents of longer duration are used.

We must now inquire whether the mere passage of a constant current is of itself sufficient to evoke contraction in a degenerated muscle. In order to determine this point the gastrocnemius in the

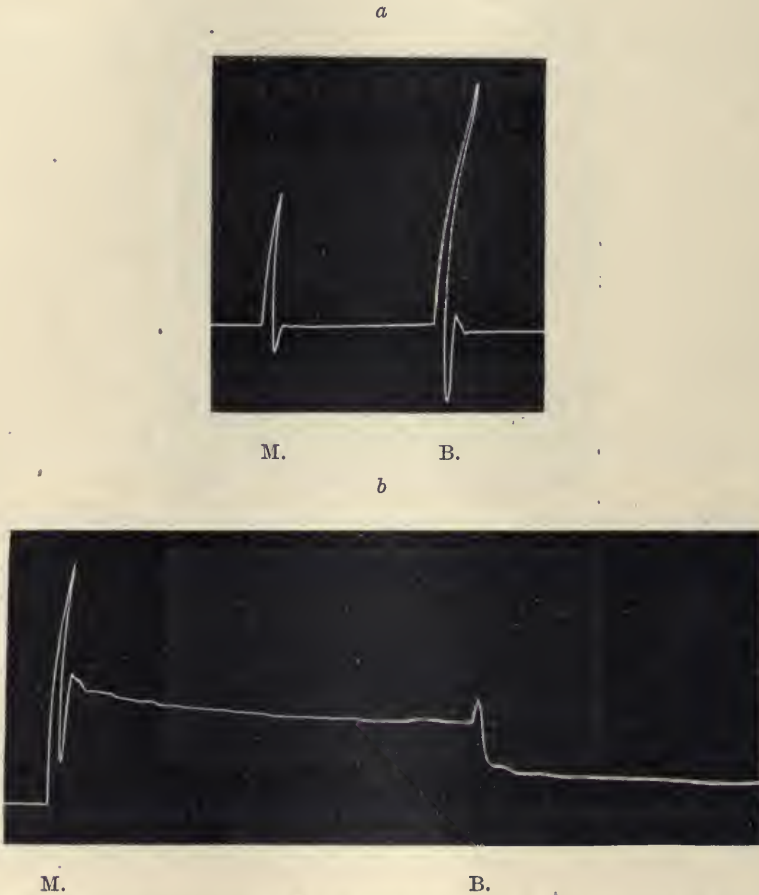


FIG. 11.—Tibialis anticus, twenty-one days after section of nerve. Upper diagram: Two induction shocks. Lower diagram: Constant current. Time: $\frac{1}{2}$ " = 1 second.

fifteenth day of degeneration is stimulated by the make of a weak current insufficient to cause galvanotonus. This causes a contraction (e.g., fig. 13). When the muscle has completely relaxed, the current is increased by lowering a resistance placed in the circuit. The muscle is unaffected. At break of the current (b) contraction occurs. The

muscle is then stimulated with a current of the same strength as at *b*. There is a well-marked galvanotonus (*c-d*). The mere passage of a current is therefore insufficient to cause contraction of a degenerated muscle. Change of potential of a certain rapidity is necessary to cause contraction, the flow of the current maintaining a condition which it cannot itself initiate.



FIG. 12—Degenerated white muscle. Strong induction shock.

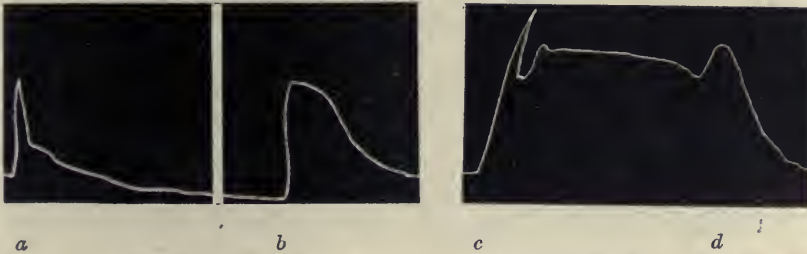


FIG. 13.—Gastrocnemius, fifteenth day. *a*, Contraction obtained by make of a weak current; the current passing through the muscle was then gradually increased; this increase had no effect. At *b* the current (now strong) was broken. *c*, Contraction obtained by make of current of same strength as at *b*. Note definite galvanotonus.

(4) *Effect of Fatigue on Galvanotonus.*

The two components of the process of contraction are capable of further differentiation. Fatigue for instance affects them unequally. If the gastrocnemius preparation be stimulated by several induction shocks in rapid succession we find that on passing in a constant current immediately afterwards the galvanotonus is still as well marked as it

was at first. If the same muscle be stimulated repeatedly by make and break of the constant current, then tonus diminishes and disappears, leaving the initial twitch unaffected. This is shown in fig. 14. Here the tibialis anticus, twenty-one days after section of the nerve, was stimulated with sixty induction shocks—this left tonus unaffected.



M.

B.

FIG. 14.—Tibialis anticus twenty-one days after section of nerve. Stimulation by constant current after stimulating with constant current about sixty times. Note fatigue effect.



M.

B.

The same muscle stimulated by constant current after stimulating with about sixty induction shocks. Note the absence of fatigue effects. Time: $\frac{1}{2}$ " = 1 second.

It was then stimulated sixty times with the constant current, the duration of the current being about one second each time. The second part of the contraction is less marked and tonus is absent, whereas the twitch at make is unaffected. The second component is therefore easily fatigued by currents of long duration, whereas it is unaffected by currents of momentary duration. By the constant current the slower contraction is more easily fatigued than the twitch.

(5) *Effect of Load.*

If we consider the effect of load upon the form of contraction we find that on the whole the effect of increasing the load is to diminish both parts of the contraction together. This is shown in fig. 15. With each load the muscle made one contraction, fatigue being thus reduced to a minimum. It will be seen that while the height of contraction at make and break is diminished, tonus is still well maintained, though at a lower level.

(6) *Combined Effect of Fatigue and Load.*

After having performed this series of weight-lifting experiments, the same muscle was then given a load of 70 gm. once more. Now the relative heights of the two components of the contraction are subject to great variation, not only at different stages of degeneration and in different muscles, but also in one muscle at the same experiment. On this occasion we see (16 a) that the maintained contraction is at a considerably higher level than the summit of the initial twitch, the summit of which is marked by the slight kink at the level B. Beyond this the lever rises more slowly until the plateau is reached. When the current had been broken the constant current was then passed in twelve times the duration, each time being about one second. Immediately

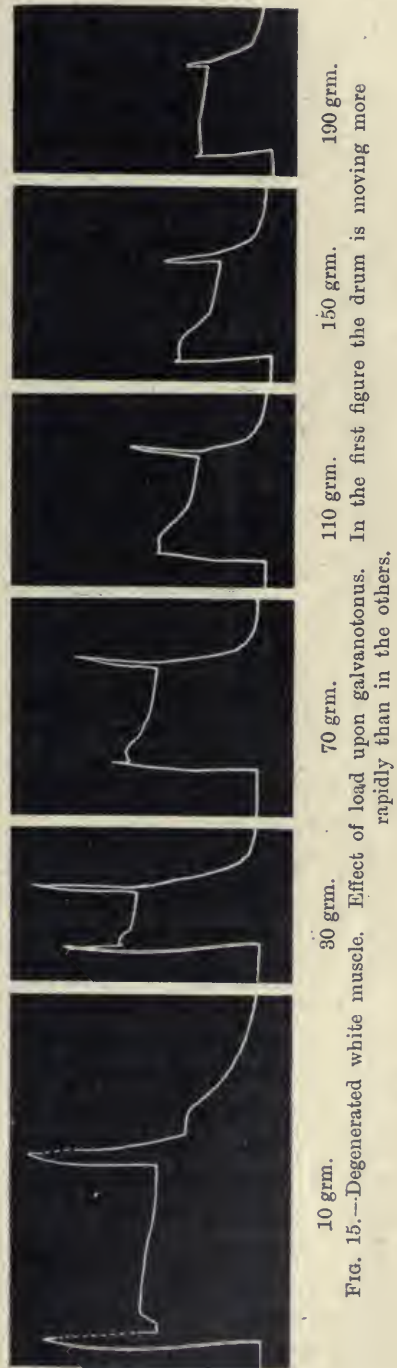


FIG. 15.—Degenerated white muscle. Effect of load upon galvanotonus. In the first figure the drum is moving more rapidly than in the others.

after this another record was taken, shown in 6 *b*. We see that there is just the initial rise ($A'B'$), which is not very different from the initial rise in the first case ($A-B$). Following this however the two curves are very different, for now the slower contraction is not as high as the initial twitch and the tonus is very considerably diminished. We see therefore that although degenerated muscle has the power of maintaining a load in the contracted state during the passage of the constant current, yet when the muscle has performed real mechanical work in lifting the load several times against gravity, this power is considerably impaired, the actual lift at make being unaffected.

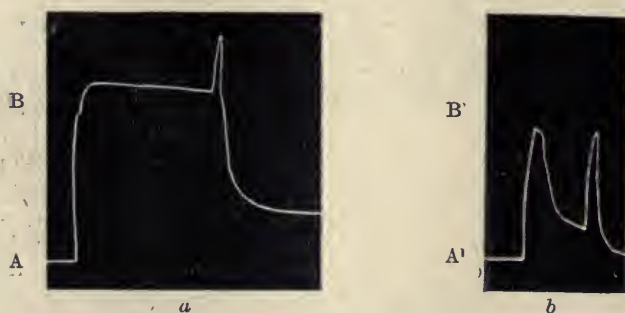


FIG. 16.—Degenerated white muscle. Combined effect of load and fatigue. *a*, Effect of constant current. Load = 70 gm. *b*, The same after passing in the constant current twelve times, the duration of the current in each case being about one second. Note the effect on tonus.

(7) *Electrical Behaviour of Red Muscle.*

In the normal red muscle a single contraction is, as we have said, more sluggish than that of the white muscle, and is preceded by a longer latent period. If a tracing be taken of the response of the soleus to a single induction shock it will be seen that the contraction is composed of two parts. This is shown in fig. 17, where the summit of the curve is seen to be distinctly double. The lever first rises quickly, though not as quickly as in the case of white muscle. It then forms a rounded summit usually a little higher than the first rise, the two being separated by a small notch. The relative heights, however, of the two components of the contraction are variable as is shown in the figures given.

On stimulating with the constant current a most curious condition is obtained. Sometimes a double contraction is obtained at make and at break resembling that which is obtained from induction shocks.

This is shown in fig. 18. Sometimes however the muscle enters at make into contraction which persists until break (fig. 19). The cause of this variation in the response of the normal red muscle I have not been able to determine. It may be an individual peculiarity, or it may

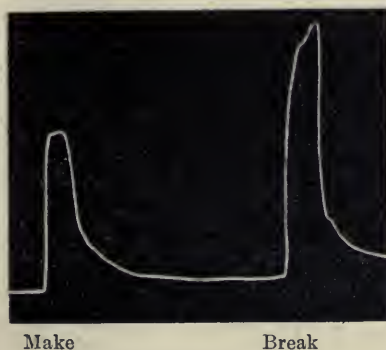


FIG. 17.—Normal soleus. Two induction shocks.

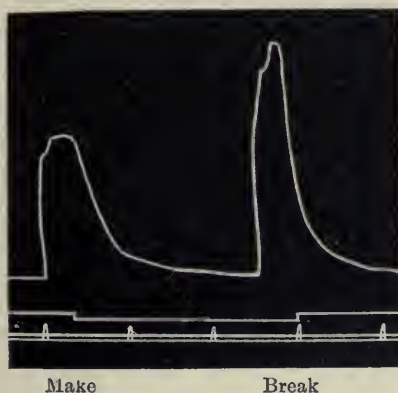


FIG. 18.—Normal soleus. Constant current. Bipolar stimulation. Time in seconds.

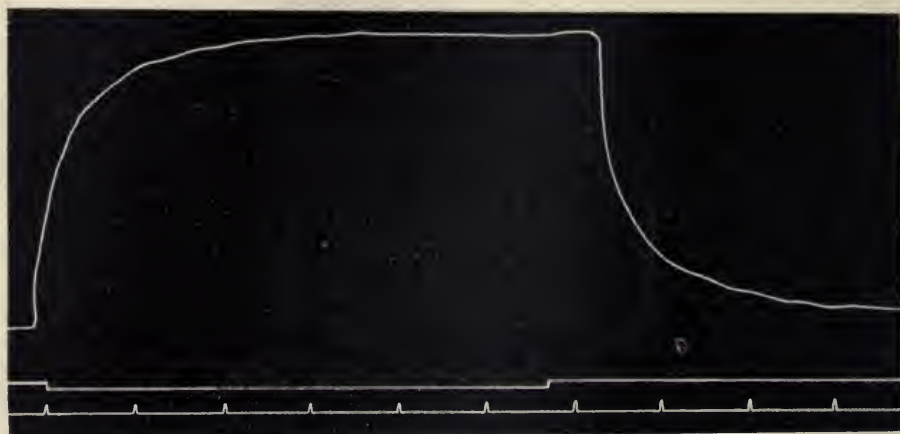
be due to the age of the rabbit. One thing is certain and that is that it is not a question of strength of stimulus. If the make and break of a constant current cause the double form of contraction, as in fig. 18, greatly increasing the strength of current will not convert this into a persistent contraction (fig. 20).

(8) *Effect of Load on Normal Soleus.*

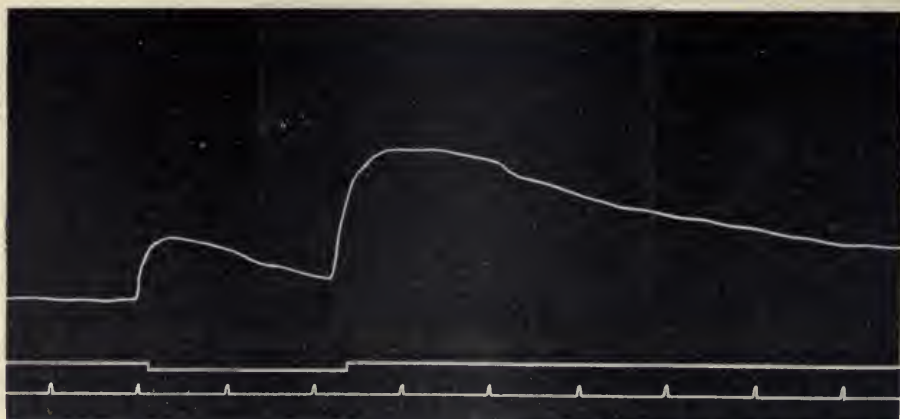
The effect of load is shown in fig. 21. It will be seen that as in the case of the degenerated white muscle increase of load diminishes the

height of contraction, but the persistent contraction is well maintained, even with 130 grm.

I have performed experiments in order to determine whether the resemblance between normal red and degenerated muscle can be pushed



a



b

FIG. 19.—Normal soleus. Bipolar stimulation with constant current. *a* = Ascending current. *b* = Descending current. Time in seconds; downstroke of the signal indicates make; upstroke of the signal indicates break.

further. Experimental difficulties have however prevented my arriving at any definite conclusion. The soleus takes origin by a small band from the posterior aspect of the tibia. On being traced downwards it is

found to be inserted for a considerable part of its length into a tendon which is common to it and to the inner head of the gastrocnemius. Through this attachment it acquires the greater part of its blood supply. When the muscle has been freed from its neighbours, an operation not

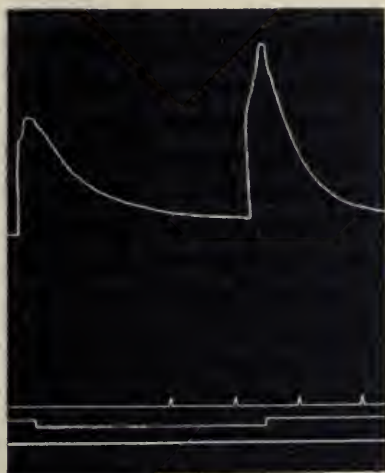


FIG. 20.—Soleus. Strong stimulation with constant current. There is a poor development of tonus.

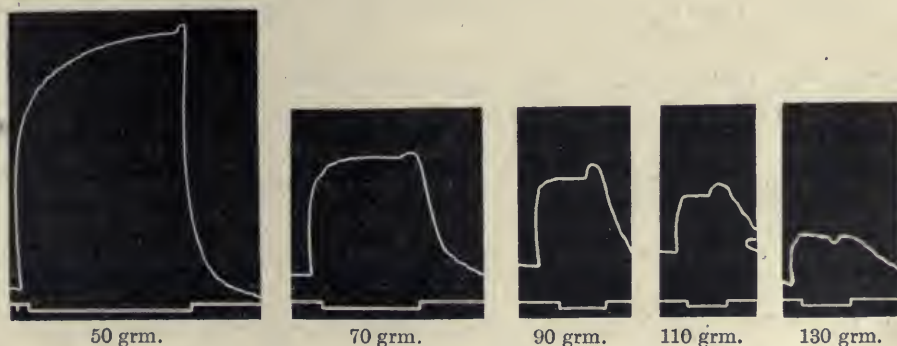


FIG. 21.—Normal soleus, showing effect of load. Bipolar stimulation; ascending current.

easy to perform without damaging its fibres, it is isolated from the circulation and soon loses its vitality. Moreover the extent to which the soleus is developed varies very greatly in different rabbits.

For the same reasons the study of the process of degeneration in this type of muscle has in my hands at any rate led to no definite

conclusion. In some cases the muscle has atrophied so quickly as to be almost incapable of contraction by the second week. Sometimes it has been possible to procure galvanotonus in the degenerated muscle when this condition was not present in its normal fellow of the opposite side.

(9) *Dual Theory of Contraction.*

The results so far obtained show that when white muscle degenerates, its electrical behaviour shows a striking resemblance to that sometimes shown by the undegenerated red muscle. Now the essential structural difference of the two varieties of muscle is as we have seen the greater amount of sarcoplasm in the red than in the white. Bottazzi [5] has argued that the two structural elements of muscle, the sarcostyle and sarcoplasm, are both capable of contraction, the former causing brisk, the latter maintained contraction. Joteyko [14] applies this theory to degenerated muscle, and assumes that the sarcostyle becomes inactive, the sluggish response being due to the sarcoplasm.

The process of reasoning which leads Joteyko to this conclusion is as follows: White muscle poor in sarcoplasm contracts briskly, red muscle rich in sarcoplasm contracts slowly—therefore the contraction of the former is sarcostylic, that of the latter is sarcoplasmic. Since red muscle degenerates more slowly than white, sarcoplasm degenerates more slowly than sarcostyle. Therefore when white muscle degenerates the excitability of the sarcostyle diminishes while that of the sarcoplasm is exalted. In my experience however there is not a particle of evidence that red muscle does degenerate more slowly than white. In most cases the reverse is true. I consider, too, that Joteyko is wrong in attributing the contraction of red muscle entirely to sarcoplasm on account of the greater abundance of this constituent in red muscle. If this were so, what is the function of the sarcostyle in this type of muscle?

It is true, I think, that the phenomena of degeneration can best be explained on Bottazzi's dual theory of muscular contraction, but not for the reasons put forward by Joteyko. Galvanotonus, as it occurs in the degenerating white muscle, is best explained on this hypothesis. There are present in muscle two contractile substances, sarcostyle and sarcoplasm. The former causes brisk contraction, the latter a more sluggish contraction, preceded by a longer latent period. In normal white muscle the sarcostyle alone responds, the sarcoplasm being relatively scanty. A single brisk contraction therefore occurs. A constant current applied

to a red muscle brings about as we have seen a double contraction, the first due to the sarcostyle, the second due to the sarcoplasm, the extent to which the second contraction occurs varying in different individuals according to the relative amount and excitability of sarcoplasm in the muscle. Presumably, when the sarcoplasm is well developed the muscle exhibits galvanotonus. The comparative slowness of the primary contraction of red muscle is the property of the sarcostyle. Sarcostyle responds to stimuli of momentary duration, such as induction shocks, while sarcoplasm is best stimulated by current of comparatively long duration. In a white muscle, when degeneration occurs, the excitability of the sarcostyle is diminished, hence the decreased response to the faradic current. At the same time the excitability of the sarcoplasm is increased, the muscle responding to the constant current by a double contraction and showing galvanotonus. The white muscle, therefore, in degeneration comes to resemble the normal red. There is indeed only one other conceivable explanation of the form of contraction obtained in the degenerated white muscle. It might be due to the process of degeneration affecting the individual fibres unequally. If this were the case the muscle at a certain period after section of the nerve should be composed of fibres in all stages of degeneration. The contraction would therefore simply be more prolonged, and would show no sharp differentiation into two parts.

That two contractile elements in the individual fibres are responsible for the changes seen in degeneration is further shown by the effect of fatigue. It has been seen that sarcoplasm is more readily fatigued than sarcostyle, but that sarcoplasm itself is fatigued as it is stimulated much more readily by current of long than by currents of short duration.

It has been shown by Parnas [21] that the postural tonus in the adductor muscle of Mollusca is associated with a gaseous metabolism, which is very little above that of the uncontracted state. Roaf [26] found that in decerebrate rigidity the amount of CO_2 formed is not appreciably greater than in paralysis due to curare. The metabolism involved in galvanotonus will be the subject of a further communication. We may note here the fact above shown that in the degenerated muscle whereas the power of maintaining a load when once it is lifted is well developed, yet after the real mechanical work of lifting the weight several times tonus is considerably impaired. In view of Sherrington's belief that postural tonus is sarcoplasmic the inability of sarcoplasm to perform mechanical work would seem to be in harmony with the results obtained by Parnas and by Roaf.

For the contractility of sarcoplasm there is abundant evidence in comparative morphology. The power of alteration of shape is present in the protoplasm of amoeba, and in all cells of amoebic form. At a stage higher in animal development we find the appearance of fibrils specially developed for the production of quick movement only. At the same time the organism still retains the power of slow contraction, the fibrils not being used in the process. This was first shown by Lieberkühn in the stalk of Stentor: "If as often happens the animals shrink slowly together during several seconds, instead of contracting suddenly, the fibrils instead of being short, thick and straight at the maximum of contraction, will be distinctly wave-like, and not perceptibly thicker than in the ordinary extended state of the animal. . . . When after slowly retracting the animals are almost globular, there is still a possibility of contraction, every fibril suddenly becoming short, thick and straight." The slow contraction is here clearly due to protoplasm.

Lieberkühn then proceeds to show the effect obtained by exposing these animals to the constant current: "While the current is passing, the protozoa usually remains in a state of contraction, but when it is weak they relax completely after a time, even during the passage of the current."

A glance at fig. 10 shows the striking resemblance in the effect of the constant current on the lowest forms of animal life, and in the degenerated muscle.

In Stentor the fibrils were seen not to take part in the slow contraction. We may argue, therefore, that in the highly complex mammalian muscle the sarcolemma, the part corresponding to the fibrils, takes no part in slow or in maintained tonic contractions, these being performed by the less highly differentiated substance.

It is interesting in this connection to compare with the process of degeneration the action of veratrin. This drug, as is well known, greatly prolongs the contraction of a muscle due to an induction shock, though it cannot itself initiate a contraction. Bottazzi believes that this drug acts by exalting the excitability of the sarcoplasm. The fact that veratrin is said to enter into chemical combination with the muscle does not negative such a theory. The effect of veratrin diminishes after the first contraction has passed off, a fact which is readily explained by the greater liability of the sarcoplasm to fatigue which the study of the degenerated muscle has led us to believe. Further, veratrin increases the excitability of muscle, resembling again the early stage of degeneration. Lastly, if a muscle be fatigued first, and then the drug applied

the excitability is increased. In this case the part which was originally fatigued is the sarcostyle, the drug acting not upon this but upon the sarcoplasm which is not fatigued, since by ordinary methods of stimulation the latter is not affected. If, therefore, Bottazzi is correct in assuming that veratrin acts specifically on the sarcoplasm, the resemblance between the veratrinized and degenerated muscle is additional evidence that the change in degeneration involves a disturbance of the normal relationship of the excitability of sarcoplasm and sarcostyle.

(10) *Function of Red Muscle.*

We have found that red muscle behaves so very differently when stimulated that we may by a short digression inquire into the function of this type of muscle. Why further are red fibres intermingled with the white in the same muscles in some animals, while in others are individual muscles composed exclusively of one kind or the other? Starling [28] shows by a comparison of the pectoral muscles of the falcon, the goose and domestic fowl, that a large proportion of red fibres is associated with the power of long distance flight. He argues from this that red fibres are developed "to carry out long-continued and powerful contractions." But if we compare experimentally the weight-lifting power of the gastrocnemius and of the soleus we find no evidence that the latter muscle is better adapted to this purpose. Moreover, so great is the size of the gastrocnemius, compared with that of the soleus, in a well-developed rabbit that it is difficult to imagine that the brunt of the heavy mechanical work falls on the soleus. If quick but light movement only were carried out by the gastrocnemius a smaller muscle would suffice.

Comparing the action of the pectoral muscles of the falcon with the corresponding muscles in the domestic fowl we find another difference besides the power of prolonged flight. The fowl performs its hurried flutter from the ground to the top of the wall by a series of rapid contractions, in which the whole of the wing takes part. On the other hand, the falcon, as Dr. Anderson reminds me, in its graceful flight, keeps the proximal segments of the wings permanently extended by tonic contraction of the pectoral muscles, while the distal segments perform the movement necessary for propulsion through the air. The pectoral muscles then being used in a different manner in the two birds, we may suppose that the difference in the two kinds of muscle fibre is associated with a different type of contraction, the white muscles for rapid, the red for persistent contraction.

Sometimes the two varieties are associated with difference in rate of movement. In the skate, for instance, Ranvier [24] has shown that the fin is moved forcibly and quickly in one direction by means of a white muscle, and slowly in the opposite direction by means of a red muscle, propulsion in one direction being thus attained.

In the case of the rabbit the anatomical relations of the red muscles are not without significance. The three best developed muscles of this type are the soleus, the crureus and the deep head of the triceps. Now if these muscles all entered into contraction at once the animal would, so far as the elbow, knee and ankle are concerned, be in a condition resembling decerebrate rigidity. It would, therefore, appear as though red muscle is concerned with the maintenance of posture. This would bring the red muscle of the mammal into line with the red pectoral muscles of the large birds. This is no red muscle to dorsiflex the ankle, because the rabbit never requires to maintain this joint in the position of active dorsiflexion. Again, from the different rate of contraction which distinguishes these muscles experimentally we may infer a similar difference of function. The even function of the tibialis anticus is to dorsiflex the foot, so that it may clear the ground while the leg is being brought forward for the next thrust. This is essentially a quick action, one cannot imagine any contingency in which the animal would have to perform this movement slowly. In flexion of the foot on the other hand we may well imagine that as this is as it were the essential act of progression a greater variety in rate of movement is required. This is provided by the presence of the two types of muscle on this side of the joint.

Another anatomical difference is this. White muscles sometimes unite bones of adjacent segments; much more frequently, however, they pass over two or more joints. The hamstrings, for instance, are attached to the pelvis and to the tibia, the gastrocnemius connects the os calcaneum with the femur, while the long head of the triceps originates from the scapula, and is inserted into the olecranon. Red muscles, on the other hand, usually unite adjacent segments of the limb, the soleus passing from the tibia to the heel, the short head of the triceps from the humerus to the ulna, and the crureus from the femur to the patella. Connected with this is the fact that red muscles always lie deeply to the white. Since white muscles which pass over two joints may cause movement at either joint, it is clear that if the full effect is to be exerted at one joint then the other one must by some means be fixed. Such fixation may be a function of red muscle. For

example, the hamstrings can either move the femur backward or they can cause flexion at the knee. But it would be impossible to get movement purely at the hip unless the knee were first fixed, and this could conceivably be done by tonic contraction of the crureus.

One further difference is to be noted between these two varieties of muscle. In some muscles the place of origin and of insertion are of small area, all the fibres passing from one end to the other. In others the attachment at either end may be of considerable extent, with the result that the fibres are of varying length. Now we find that speaking generally the white muscles belong to the first class. In the case of these muscles which pass over two joints especially. The red muscles belong to the second class. In the rectus femoris, for instance, most of the fibres arise from the pelvis and are attached to the patella; there is very little tendon insertion. The subjacent crureus, however, arises from a considerable area involving almost the whole of the anterior aspect of the femur. Consequently the fibres vary very considerably in length.

Now Lucas [18] has shown that in the case of amphibian muscle the fibres individually obey the all-or-nothing law as in the case of the heart. That is to say grading of contraction is brought about, not by variation in the amount of shortening of each individual fibre, but by varying the number of fibres brought into play. If this rule holds also for mammalian muscle, concerning which we have as yet no information, we can readily imagine that for graded movement the arrangement found in the red crureus is far superior to that found in a muscle of parallel fibres such as the rectus femoris.

In higher animals such as man we find that the red and white fibres are found not in separate muscles but in each individual muscle. Associated with this is the higher power possessed by man of performing a movement of accurately graded intensity in almost every muscle.

The functions of red fibres would then appear to be: (1) to play a prominent part in maintaining posture; (2) to perform slow movement; (3) to perform movement of graded extent; (4) to act synergically with white muscles which act upon two joints by fixing one joint, thus enabling the white muscle to act solely upon the other. Red fibres do not appear to be well adapted to perform mechanical work of a heavy nature.

Summary of Chapter V.

(1) The reaction of degeneration in mixed human muscle cannot be attributed to a more rapid death of the white fibres.

(2) White muscle at a certain stage of degeneration resembles very closely normal red muscle in its electrical behaviour.

(3) This is adduced as an argument in support of the theory that the brisk twitch of normal muscle is a contraction of sarcostyle, while the slow contraction of degenerated muscle is due to sarcoplasmic activity, the sarcostyle degenerating more rapidly than the sarcoplasm.

(4) Morphological and pharmacological evidence has been given for the contractility of sarcoplasm.

CHAPTER VI.—ELECTRICAL REACTIONS IN CONDITIONS AFFECTING MUSCLES PRIMARILY.

We have seen that the process of degeneration is the result of damage to the motor nerve or nerve cell. Changes in the electrical behaviour of muscles also occur in those obscure conditions in which the seat of the lesion appears to be not the nerve but the muscle itself. At the present day three such diseases are recognized—myasthenia gravis, myotonia congenita and amyotonia congenita.

(1) *Myasthenia Gravis*.

Myasthenia gravis is distinguished clinically by the readiness with which fatigue occurs. Histologically the muscles involved and certain other organs are the seat of lymphorrhages. According to Farquhar Buzzard [6], electrical examination shows that with the faradic current the muscles are readily fatigued and soon cease to respond. If the constant current be applied to a muscle thus fatigued, a brisk normal contraction is the result. According to other observers the behaviour of the muscles to the two forms of current is variable; sometimes cases occur in which fatigue is produced by the constant more readily than by the interrupted current. It is extremely difficult to see how this can possibly be the case unless, which is quite possible, the interrupted current used in the examination was far stronger than the constant current.

Buzzard has suggested an explanation of his results based upon Bottazzi's dual theory. He supposes that the condition is due to a failure of the sarcoplasmic element in the muscle fibre. But this hypothesis would only hold good if the sarcoplasm were normally more resistant to fatigue than the sarcostyle. This seems to be disproved by the experiments above described. Further, the paralysis of the sarco-

plasm does not explain why the fibre retains its excitability to the constant current when fatigued apparently to exhaustion by the interrupted current. If the contraction obtained by the constant current

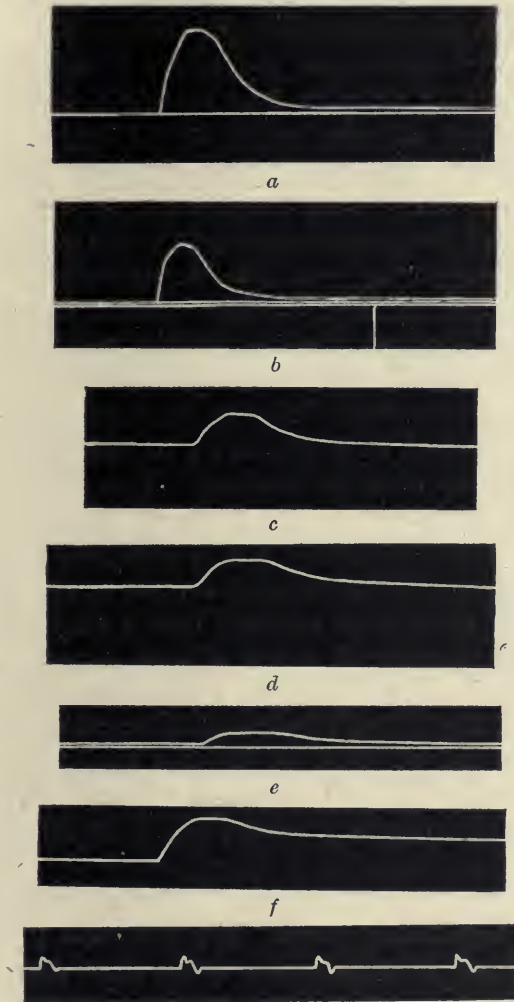


FIG. 22.—Muscle. Gastrocnemius of frog. *a*, Make of constant current. *b*, Single induction shock. *c*, *d*, and *e*, Induction shocks in stages of fatigue by the interrupted secondary current. *f*, Make of constant current immediately after *e*. Note the contraction is not as good as the initial one *a*, but is well marked and still brisk, as a comparison with the time record below ($\frac{1}{3}$ second) shows.

under these conditions were sluggish, resembling that which is obtained in the degenerated state, one might argue that in myasthenia gravis there is a pathological condition affecting the sarco-sylic element,

rendering it abnormally liable to fatigue. But this is not the case. The problem before us is to explain why the muscle, though no longer responding to the faradic current responds in an apparently normal manner towards the constant current.

It is well known that the physiological efficacy of a current depends upon two factors—intensity and duration. A current of a certain strength of momentary duration may be totally ineffective, whereas a current of the same strength lasting for a longer period may cause a normal contraction. The two factors, intensity and duration, are related to one another inversely, the stronger the current the shorter the minimal period necessary to produce a physiological effect and vice versa. Now supposing a muscle be stimulated repeatedly by a current of certain strength and duration. Sooner or later the muscle, whether healthy or diseased, becomes fatigued and ceases to respond. But when this condition is attained the muscle can be made to contract by using a stronger stimulus. This can be done either by increasing the voltage of the current or by prolonging its duration. In this way a fair response can once more be obtained. This can be easily shown by the following experiment: The frog's gastrocnemius is dissected out and the distal end connected with a recording lever. It is first stimulated by the make of the constant current (*a*, fig. 22). It is then tetanized until the contraction obtained from a single induction shock is very feeble and sluggish (*b*, *c* and *d* show stages in the process). It is now once more stimulated with the constant current. A current stronger than that used before tetanization is required, but the resulting contraction, while not as sharp as the first contraction obtained (*a*), is nevertheless far better than the slow response obtained from the induced current. As observed by the eye it would undoubtedly be considered brisk.

We see therefore that the normal muscle behaves in the same way as the muscle in myasthenia gravis. The difference is one of degree, fatigue being induced far more rapidly in the latter than in the former. The explanation of the reactions in myasthenia gravis would therefore appear to be perfectly simple. The phenomena are due to an abnormal proneness to fatigue, which when it has once appeared affects the muscle in the same way as it does normal muscle. It is thus not necessary to assume that one histological element is affected more than the other.

(2) *Myotonia Congenita*.

In this condition all movements are first performed very slowly, and there is considerable difficulty in relaxing the muscles. With repetition

the contraction loses its sluggishness and eventually becomes as brisk as the normal. After a short rest however the sluggishness returns. Histologically there is a very striking increase in the size of the fibres, which may be from twice to four times as wide as normal. Transverse striation is but feebly marked and the nuclei of the sarcolemma are increased.

Electrical stimulation of the nerve trunk causes a prolonged contraction of the muscle. Similarly when the muscle itself is stimulated the resulting contraction is sluggish. In extreme cases it may last as long as half a minute. The muscle can be stimulated by K.C.C. and A.C.C. indifferently.

The clinical picture in this condition reminds one very forcibly of the action of veratrin, more especially in the prolonged relaxation. Possibly the hypothesis which Bottazzi brought forward to account for the action of the alkaloid may apply to this condition also, that is to say, there is an abnormal development in the amount and excitability of the sarcolemma. On stimulation it is the sarcolemma and not the sarcostyle which first responds—hence the sluggishness. The increasing briskness on repetition of the contraction is further evidence in support of this, for we have seen reason (Chapter V) to believe that the sarcoplasm is more quickly fatigued than the sarcostyle. As the excitability of the sarcoplasm decreases, the stimulus affects more and more the sarcostyle which is responsible for the brisk contraction ultimately obtained. That there is such a disturbance in two contractile elements is further indicated by the histological appearance of a muscle thus affected, the feebleness of the cross-striation indicating a comparatively poor development of the sarcostyle.

CHAPTER VII.—WASTING.

Wasting is so characteristic a feature in a muscle separated from its nerve-cells that it must be regarded as an essential part of the change which constitutes degeneration. It must be borne in mind, however, that this is not merely due to what is commonly called disuse, atrophy, though want of movement is no doubt responsible for some of the loss of substance involved. In the first place, atrophy due to disuse though in long-standing cases it may be extreme, never occurs so rapidly as the atrophy following nerve section. In a case of ulnar paralysis of about two months' history, the dorsal interossei will be found to be extremely wasted. But the small muscles of the hand, which are supplied by the

median, will present a striking contrast, even though the hand has been completely immobilized. If we use the term "disuse atrophy" in a broader sense, implying atrophy due not only to want of movement but also to want of tonus, then disuse may account for a still greater amount of the wasting which occurs. On the other hand, in paralysis due to causes other than nerve injury, however far advanced the wasting is, the electrical changes, characteristic of nerve injury, never develop. The atrophy of degeneration is therefore something more than the loss of substance due to want of exercise.

In the experiments described in Chapter V, I have weighed the muscles used—namely, the gastrocnemius, soleus and tibialis anticus—and have compared them with the corresponding normal muscles of the opposite limb. My first object was to find out whether there was any difference in the wasting of red and of white muscles, for it had been asserted that the former degenerated more slowly than the white. In the case of the soleus the muscle is so small in some animals, especially when degenerated, that it is not easy to weigh it with any accuracy. The difficulty is further increased by the peculiar insertion of the muscle, already noted above. The part of the tendo achillis into which it is inserted belongs chiefly to the gastrocnemius. In order to get the true weight of the soleus I have first freed the muscle from its tendon.

TABLE VI.—SHOWING AMOUNT OF WASTING.

No. of Rabbit	No. of days after section of nerve	GASTROCNEMIUS			SOLEUS			TIBIALIS ANTICUS		
		Normal	Degenerated	Percentage difference	Normal	Degenerated	Percentage difference	Normal	Degenerated	Percentage difference
1	3	8.83	7.64	13.5	0.87	0.71	18.4	3.12	2.82	9.6
2	8	10.97	7.30	33.5	1.00	0.77	33.0	3.82	3.39	11.25
3	10	8.10	7.33	10.2	1.30	0.74	43.0	4.02	3.91	2.7
4	14	10.00	6.90	31.0	1.20	0.85	29.2
5	14	11.34	8.50	25.0	1.49	1.30	13.0
6	15	16.70	10.65	36.0	1.60	1.32	17.5	5.75	4.80	16.5
7	21	10.90	6.50	40.0	0.7	0.9	..	3.27	3.50	..
8	30	15.35	6.80	55.4	1.22	0.37	69.7	5.60	3.50	37.5
9	34	8.84	4.04	54.3	0.72	0.67	6.9	4.12	2.23	45.9
10	53	10.25	6.07	40.0	0.97	0.52	46.4	4.05	2.75	32.1
11	58	13.07	5.22	59.8	1.45	0.47	67.6	5.30	2.75	48.1
12	70	6.75	4.95	26.7	0.73	0.27	63.0	2.10	1.75	16.7

The figures given in Table VI bring out one point very clearly, and that is the great variation to which wasting is liable. In one case

twenty-one days after nerve section the muscles on the paralysed side were actually heavier than the corresponding muscles. They may of course have been considerably heavier before the operation.

It has been customary among advocates of electrical treatment who wish to give a practical proof of the utility of artificial stimulation to demonstrate the increase in weight obtained in rabbits' muscles, unstimulated muscles being used as a control. Lewis Jones, for instance, used this method as a proof of the superiority of sinusoidal over the ordinary galvanic current. Recently Langley [16] has been unable to find any difference in weight as a result of stimulation. In these experiments the constant current and the condenser were used, the muscles being stimulated, some for short, others for prolonged periods daily. From my own experiments I am convinced that so great is the variation in wasting to which muscles are liable that experiments in which loss of weight is taken as the standard are of very little value. So far as my figures go they would appear to indicate that there is no great difference between the wasting in red and in white muscles. On the whole the former atrophy rather more quickly than the latter. If then the amount of wasting is any guide to the amount of degeneration, there is no evidence that red muscles degenerate less rapidly than white.

The results obtained, however, illustrate one point of a more positive character. It will be seen that the *tibialis anticus* in all cases wastes less than the *gastrocnemius*, in many cases the difference is considerable. Now it is well known that when the sciatic nerve is injured in man the anterior tibial group is affected to a greater extent than the muscles of the calf. Sherren [27] suggests that it is due to the more exposed position of the fifth lumbar root, and of the external portion of the great sciatic nerve in the thigh. But this does not explain the fact that the same difference is found in paralysis due to toxic neuritis. Hofman makes the improbable suggestion that the external popliteal nerve is more vulnerable, because it receives a smaller branch of the *comes nervi ischadici*. Now it has been well known to surgeons that so long as a paralysed muscle is stretched it will not recover. Neurologists and surgeons alike have drawn attention to the importance of keeping a paralysed muscle in a relaxed condition. This has again been very recently insisted upon by Robert Jones [13]. There seems no doubt, therefore, that stretching involves a considerable amount of damage. In slight injuries or affections of gradual onset, such as neuritis involving the sciatic nerves, the nerve may be affected as a whole, causing

paralysis of both muscle groups equally. As the patient continues to walk about, a new factor comes into play—namely, the weight of the foot. By this means the anterior tibial muscles are stretched while the gastrocnemii are released, hence the damage already done by the nerve injury is increased in the former, and diminished in the latter. If the patient lies in bed, the weight of the bedclothes on the toes acts in the same way unless specially guarded against. Drop-foot of toxic origin would therefore appear to be due, not to an affection of the external popliteal part of the sciatic, but to the stretching of the anterior tibial group after a generalized inflammation of the whole nerve. The same explanation accounts for the unequal fate of the two sets of muscles following wounds of the sciatic, a fact which has been noted both in the South African War and in the great war of the present day.

That this explanation is probably correct is confirmed by the relative wasting of the tibialis anticus and gastrocnemius in the rabbit. In this animal, as it feeds quietly in its cage, the hind legs are in a position of dorsiflexion, whether the sciatic nerve is cut or not. The gastrocnemius is thus subject to constant stretching, whereas the anterior tibial muscle is completely relaxed, hence the greater atrophy of the former than the latter.

The experimental results, therefore, strengthen the conviction of the overwhelming importance of keeping the muscles relaxed.

Summary of Chapter VII.

(1) The amount of wasting is so variable in the rabbit that any experiments in which loss of weight is adopted as a measure of degeneration are of little value.

(2) There is no great difference in rate of wasting between white and red muscles. In the majority of cases the red atrophied more than the white.

(3) In the rabbit the gastrocnemius wastes more than the tibialis anticus; this is explained by the stretching of the former and the relaxation of the latter in the position of dorsiflexion normal to these animals. In man the weight of the foot produces the reverse result, thus explaining the greater affection of the muscles of the front of the leg than of those of the calf.

CHAPTER VIII.—CONCLUSIONS.

(1) The normal muscle responds to the faradic current, whereas the degenerated muscle does not. To the galvanic current the normal response is brisk, the pathological is slow or vermicular.

(2) When the process of degeneration has lasted a month the degenerated muscle is less excitable than normal to the constant current.

(3) In normal muscle K.C.C. > A.C.C. so long as the testing electrode is placed on the motor point, this is not always possible in the case of small muscles. In the degenerated state the muscle tends to be indifferent to polarity; differences may exist in either direction, but these are small in comparison. In a normal muscle the K.C.C.: A.C.C. increases with increase of stimulus, in degeneration the relationship is not varied by increase of stimulus.

(4) Normal muscle is more excitable at its motor point than at any other part. Degenerated muscle is equally excitable at all points on its surface.

(5) In cases of peripheral nerve injury there is usually no doubt as to whether the muscle is degenerated or not. The question of practical importance is the extent of the injury which the nerve has suffered. To this question it must be admitted electrical reactions give but a limited answer, the chief reason being that the electrical response does not go *pari passu* with voluntary power. It cannot be too strongly insisted that the testing of the muscles is one only of several methods by which we can estimate the condition of the nerve. It is not the purpose of this thesis to discuss these methods, but we may enumerate them here. They are (i) the sensory loss, (ii) the trophic changes, that is to say the condition of the hair, nails and skin, and (iii) the degree of wasting. In cases of gunshot wounds of nerves, if the full reaction of degeneration is given by wasted paralysed muscles, if the sensory loss is full and trophic changes well developed, exploratory operation is advisable without delay provided the wound is aseptic. And this for two reasons: first, the small risk of the operation; second, the long period which must elapse before any objective change occurs if a waiting policy is taken. Cases in which the muscles give the reaction of degeneration where the wasting is slight, where the sensory loss is not complete, and when the trophic changes are not developed should be watched first for a couple of months or so. Injuries of this class usually recover without operative interference. These are the two

main types of nerve injury met with in the present war. Cases of an intermediate type, of course, occur. My own practice has been in such doubtful cases to advise operation. I may say that in a very large number of cases I have had reason to regret my decision in one only.

(6) This brings us to the question of subsidiary treatment by electricity and massage. Langley [16] has attempted to show by experimenting on rabbit's muscles that daily stimulation is useless. I have already shown that the results obtained in this way are inconclusive, and altogether beside the point. The results must be obtained from man. It is, of course, impossible to obtain any absolute proof by this method, but one has only to compare a limb which has been well cared for by constant stimulation with one which has been neglected, to be convinced of the value of electrical treatment in these cases. How the current acts is not certain. We may suppose that just as passive movement improves the condition of an affected joint by breaking down adhesions and exercising the muscles, so constant internal movement of the muscle itself maintains a condition of mobility in the sarcoplasm, and prevents fibrosis during the regeneration of the sarcostyle.

As to the form in which treatment should be administered I consider the constant current interrupted by a metronome to be the best. This should be done for at least fifteen to twenty minutes daily. Care must be taken that the current does not spread so as to stimulate the healthy muscles of the opposite side of the limb. If this is done the paralysed muscle is damaged by being stretched. For this reason the method of immersing the whole limb in an electric bath is strongly to be deprecated. The greater spread of current which occurs when the condenser is used makes this instrument less efficient as a means of treatment than the interrupted constant current. I have already insisted upon the importance of keeping the paralysed muscle permanently relaxed.

The clinical data of the above work were obtained from patients at the First Eastern General Hospital, Cambridge; the experimental portion at the Physiological Laboratory of the University. The expenses were defrayed by the Medical Research Committee, whose secretary, Dr. W. M. Fletcher, I have to thank for suggesting the experimental part. I am indebted also to Dr. H. K. Anderson, for the interest he has taken in the research, and to Mr. J. Barcroft for kindly facilitating work in a laboratory much depleted of assistants.

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ON DISTURBANCES OF THE LOCALIZATION AND DISCRIMINATION OF SENSATIONS IN CASES OF CEREBRAL LESIONS, AND ON THE POSSIBILITY OF RECOVERY OF THESE FUNCTIONS AFTER A PROCESS OF TRAINING.

(I) PARTIAL RECOVERY OF THE ACCURACY OF LOCALIZING TACTILE STIMULI, TOGETHER WITH A DISCUSSION OF THE FACTORS WHICH UNDERLIE THE PROCESS.

BY T. GRAHAM BROWN

AND

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I.—INTRODUCTION.

It has been known for some time that recovery of function may take place after a lesion of the so-called "motor" area of the cerebral cortex in the higher mammals—although for a time after the infliction of the lesion there occurs paralysis of "voluntary" motion of the parts of the opposite side of the body which were served by the area destroyed.

The possibility that recovery of function may take place in a similar way after a destructive lesion of the so-called "sensory" area of the cerebral cortex is a question which has hitherto received little attention.

Such an investigation would be difficult (although perhaps not impossible) to perform in animals. It is obviously more easy to make in the case of man, but suitable cases are rarely encountered in civil practice. At the present time, however, much material for its prosecution is being provided by gunshot wounds of the cerebrum. Although we have had access to but few organic cerebral cases, of late we have been fortunate enough to have two such cases under our observation.

Although little or nothing is known of the manner of working of the mechanism in the cortex cerebri, it seems probable at any rate that the paths by which the impulses which subserve sensations are carried to the cortex are more complex than those which carry the so-called "motor" impulses for "voluntary" action away from it.

Head and his co-workers have shown that probably the afferent impulses which subserve the different forms of sensation conditioned by stimulation of end-organs in the skin and deeper structures are re-arranged in the spinal cord at or near the level of entry of the nerve-fibres which carry them. A second re-arrangement takes place at the level of the nuclei of the posterior columns of the cord in the medulla oblongata, while a third re-arrangement occurs at the optic thalamus.

In the spinal cord the afferent impulses which subserve the sensations of pain, of heat and of cold cross to the opposite side of that organ soon after their entry and then are carried upwards in secondary nerve-paths upon the side opposite to that from which they entered. The afferent impulses which subserve postural recognition and spatial discrimination run upwards upon the same side of the spinal cord as that of their entry. They travel along primary nerve-fibres in the posterior columns of the cord. The afferent impulses which subserve contact sensibility seem to travel upwards in a double path—partly on the same side and partly on the opposite side of the spinal cord to the side of entry. These impulses are evoked by touch and by pressure; this group carries with it the impulses which underlie the power of recognizing the situation of the stimulated spot.

At or above the level of the nuclei of the posterior columns of the cord the paths which carry the afferent impulses which subserve the sensations of pain, heat and cold run unaltered upon the opposite side of the brain stem to the optic thalamus; save only that there appears to be a certain degree of independence between the paths for the impulses

associated with these three sensations. The primary nerve-fibres which carry the impulses for postural recognition and spatial discrimination end in the nuclei of the posterior columns. Thence these impulses are carried upwards to the optic thalamus in two independent secondary paths—one for the impulses which subserve postural recognition and one for those which subserve spatial discrimination. The other uncrossed afferent paths now cross over to the side of the central nervous system opposite to that on which they entered.

According to the views of Head and Holmes [1], these various afferent paths—all now secondary—end in the optic thalamus where yet another redistribution takes place. From an examination of clinical material these observers believe that in the optic thalamus there is, besides the group or groups of nerve-cells at which all the afferent secondary nerve-fibres end, a mass of grey-matter which they term the “essential organ of the optic thalamus.” This, they suppose, forms the centre for certain fundamental elements of sensation. Its activity is mainly occupied with the affective side of sensation, and it is the “centre of consciousness” for certain elements of sensation—responding to all stimuli which are capable of evoking either pleasure and discomfort or consciousness of an internal change in state. The afferent impulses which subserve these sensations are presumably carried in short tertiary nerve-fibres from the nerve-cells at which the secondary nerve-fibres end to those in the essential organ of the thalamus.

Besides these short intra-thalamic tertiary nerve-paths there are, they suppose, longer tertiary nerve-fibres which carry on other afferent impulses from the nerve-cells at which all the secondary afferent fibres end in the thalamus to the cortex cerebri. These afferent impulses have been re-arranged in the optic thalamus and now run in five distinct paths—that is, in five paths, any one of which may be affected separately by a cerebral lesion. These five groups are: (1) the afferent impulses concerned with the recognition of posture and passive movement, and subserving the secondary faculty of discriminating weights on the unsupported hand; (2) those which subserve certain tactile elements (and also the discrimination of weights on the supported hand); (3) those which subserve spatial discrimination (the appreciation of two points applied simultaneously to two different points on the surface of the skin, and also the recognition of the size and shape of objects which are in contact with the skin); (4) those which subserve the power of localizing the situation of a stimulated spot of the skin, and that of the recognition of the double nature of two points applied

consecutively to too different spots on the skin ; (5) those which subserve a scale of sensations with heat at the one end and cold at the other.

These observers believe that out of such materials the cortex cerebri fabricates the sensations for which it is responsible. They think that a great function of the cortex is the power of relating one sensation with another.

Now, if an object from the outside world comes into contact with a flat area of the skin the resultant stimuli engender afferent impulses which ascend in the central nervous system and finally subserve sensations of different kinds. These may be interpreted in consciousness in different manners. The relative hotness or coldness of the object, its roughness or smoothness, its size and shape, its weight and the part of the skin with which it is in contact, may all thus be perceived if we take a specific area of the skin, and apply tactile stimuli to spots within it ; these stimuli may finally give rise to sensations which give information with regard to the locality of the touched spot within that area, or with regard to the doubleness of the touches if two different spots are touched either simultaneously or successively, and so on.

After certain cortical lesions the interpretation of these sensations may be greatly interfered with, and the description by the patient of the sensation (for instance, with regard to the localization upon the skin of a spot which has been touched) may be confused and wrong, or he may not be able to describe it at all.

The interesting question arises, whether in such a case it is possible to "educate" or "train" the patient in such a manner that his replies to questions of this nature become accurate. Head and Holmes state that even twenty-three years after certain cortical lesions there may still be complete loss of the power of discrimination of two different points upon the affected side (compass-test), grave disturbance of the power of localization of tactile stimuli, and abolition of the power of appreciation of size, shape, and form in three dimensions, and of the power of recognition of familiar objects.

As far as we know, no attempt has hitherto been made in such a case to "re-educate" the lost faculties. The patient can hardly be expected to do this himself unless definitely directed to do so. For all practical

¹ We prefer the word "training" to signify a process by means of which such a lost cortical (or cerebral) function as that of localization might possibly become restituted. This word appears to us to have a more neutral meaning than "education" or "re-education," and to avoid committal to any theory with regard to a change which may possibly take place.

purposes his recognition of these attributes of objects is easier performed by sight (and, of course, by the unaffected hand), and there is little or no necessity for the "training" of recognition through the persisting sensations from the affected limb.

But if a definite effort is made is this "training" possible? If it is certain further questions of interest are raised. What are the factors which condition the appearance of improvement? Is it permanent or transient? Is it partial or complete? Again, suppose that it is possible to "re-educate" a lost faculty of the localization of tactile stimuli for certain definite spots on the skin, does the "re-education" affect the relative accuracy of the localization of tactile stimuli for other (let us say, neighbouring) spots which have not directly been "re-educated" for this faculty? Does a possible betterment of the localization of tactile stimuli for these specific spots which have been directly trained affect the accuracy of localization for other kinds of stimuli (that is, heat, cold, pain, &c., as well as other degrees of tactile stimuli than that used in the "re-education") for the same specific spots? And are other forms of sensation affected?

These problems are investigated in the experiment described in this paper. Before we attack them certain points in connection with the localization of cutaneous sensations may be considered.

II.—ON DISCRIMINATION AND LOCALIZATION OF TACTILE SENSATIONS.

When the normal subject of an experiment is so placed that he is unable to see a specific area of his skin—for instance, that of the palmar aspect of a finger—and a supra-liminal touch stimulus is then applied to a spot within it, he is able at once accurately to point to the corresponding spot on the hand of a model, although the only peripheral data which he receives are those of the touch stimulus itself.

The stimulus sets into action certain receptive end-organs in the spot of skin and underlying tissues. Thence afferent impulses pass into and up through the central nervous system until (probably) they effect activities in the cortex cerebri. There a complex physiological process occurs, the final resultant of which is the activation of certain "motor" mechanisms which in the end condition a very accurate movement of the hand which indicates the corresponding position of the touched spot upon the model. Parallel with the cortical changes there are changes in consciousness. The sensation conditioned by the stimulus is perceived; and, with it, various attributes of which the locus of the stimulus upon the surface of the body is one.

In the conditioning of the accuracy of this localization of the touched spot we may discern three factors.

In the first place, the sensations conditioned by the tactile stimulus must in some manner be different from those conditioned by all other tactile stimuli which are applied to other spots of the skin. This attribute of the sensation conditioned by tactile stimulus may be termed (for convenience here) its "character." It is clear that, if there was no such difference between the sensations which are conditioned by, or accompany, differently located tactile stimuli, accurate localization of any one of them would not be possible.

In the second place, the sensations conditioned by the tactile stimulus must in some manner be like those conditioned by all previous tactile stimuli which have been applied in the past to the spot which is now touched; and, moreover, it must also be like the sensations conditioned by other previous stimuli, such as those of pain, heat, or cold—for if one of these is applied to this spot it is also accurately localized there. This attribute of the sensations conditioned by the stimulus may be termed its "individuality." It is clear that if the sensations conditioned by different tactile stimuli which are applied at different times to the same spot have not a common "individuality" accurate localization of any one of them would not be possible, and the subject at one time might localize the stimulus in one place, and at another time in another place.¹

These attributes of the sensation conditioned by a tactile stimulus are not, however, in themselves sufficient for the exact localization of a touch. The character of the touch may serve to distinguish it from all other touches which are applied to other spots, and its individuality may serve to liken it to all previous touches which have fallen on the same spot. The resultant localization might still be impossible or, although a constant one, it might be inaccurate. That is to say that the subject might localize a touch which is applied to a certain spot on the palmar surface of one of the fingers of his right hand at a dissimilar spot on the palm of the model, thinking that that spot corresponded in

¹ In this paper we use the term "location of the stimulus" to express the act of the observer in applying the stimulus to a certain spot on the body of the subject; or to express the locus of that stimulus as it appears to the observer. We use, on the other hand, the term "localization of the stimulus" (or "of the spot," or "of the sensation conditioned by the stimulus"—indifferently) to express the cerebral process whereby the subject finally indicates the position which he thinks that the touched spot occupies. We do not go into the question whether the subject localizes the stimulus, or the sensation conditioned by it, but use the two forms of expression indifferently.

position to the spot on his own finger which was touched. Each time that spot is touched on his own finger he may locate the touch on that one dissimilar spot on the palm of the model. In such a case the localization of the tactile stimulus would be constant, but it would be inaccurate.

A third attribute of the touch must therefore be its topographical position upon the surface of the body. This we may term its factor of "position."

These three hypothetical attributes of the touch—its character, its individuality, and its position—are not mere refinements of analysis. Their consideration has a very direct bearing upon the problem of errors of localization and of discrimination of tactile stimuli.

The effect of a certain lesion of the cortex cerebri may be to destroy the faculty of localization of a touch. That touch may still be perceived in consciousness as such, but the patient may be unable to refer it (or to refer it accurately) to the corresponding spot on the model (that is, to the "similar" spot on the model) if he is unable to see the spot which has been touched.

Now in such a case the subject may be unable to localize the touch at all. As in many of the cases cited by Head and Holmes, he may be "confused" when he is asked to point to the corresponding spot on the body of the model. He is completely ignorant of its location. There is no question here of the character, individuality, or position of the touch; the subject is, as it were, "cortically blind" to localization—just as "cortical blindness" is associated with certain lesions of the cerebrum.

But the subject (in other cases) might still think that he is able to localize the touch. In such a case he may make the attempt to localize it; but each time he is wrong in his localization. Touches which are applied at different times to one and the same spot of the subject's skin may be localized by him at different spots on the model; and different touches on the subject may, at different times, be localized upon the same spot on the model. In such a case the faculty of localization may be said to be "impaired" or to be "abolished" for certain areas of the skin—but it is evident that the condition is a different one from that in which the subject is unable to make any attempt at localization of the stimuli. That is, of course, if it is certain that the subject is not merely guessing the positions of the stimuli.

In a case in which the subject thinks that he can localize his tactile stimuli the ordinary methods of examination yield results of little value for the analysis of his condition. It is not sufficient for the observer to

touch one of an infinite number of spots on the subject's hand, and to note simply that the spot is wrongly localized upon the model. Information is needed with regard to the wrongness of the answers. It is needed for data with regard to the question whether a touch which is applied to a certain specific spot is always referred to the same (wrong) position on the model; and whether that same position on the model is sometimes indicated as the corresponding location of touches which are applied to other spots on the subject.

In an ordinary test of the function of localization of touches the area investigated is usually restricted. That is to say, that the subject usually knows that the stimulus will be applied to a spot on a certain restricted area of the skin—for instance, to the skin of the hand, or to that of the arm, and so on. If a further restriction is made, and the subject is allowed to know that the stimulus will be applied to one of a definite small number of spots upon (let us say) his hand, the conditions of the experiment are such that information with regard to the manner of the wrongness of localization of touches may be obtainable.

Now, if the character of the sensations conditioned by tactile stimuli applied to our chosen spots is lost, the subject may refer the locus of a stimulus which falls upon one of them to a certain spot on the hand of the model. It is theoretically possible that he may think that he has made an accurate localization of it; but when a certain other spot is touched he may also refer the locus of that touch to the same spot on the model, and still think that the localization is accurate. In other words, he may think that the two different tactile stimuli are applied to the same spot, whereas, in fact, they are applied to different spots. If the character of the touches is lost for spots in a certain area of the skin it might be thought that the attributes of individuality and posture would be lost at the same time. This is, perhaps, not necessarily the case. Thus the touches applied to spots in that area might lose their attribute of character—so that they would seem all to have the same locus. The touches become similar, and at the same time the attribute of individuality of the different touches would merge in a common individuality. This is not the same as a loss of the attribute of individuality; we might say, perhaps, that difference of individuality is a function of the characters of sensations conditioned by differently located tactile stimuli. When the attribute of character is lost the attribute of individuality may become a common one for sensations conditioned by tactile stimuli applied to the spots in this area. In a similar manner, the attribute of position might possibly also persist

even after the loss of the attribute of character. Thus the differences of individuality of the sensations conditioned by tactile stimuli which are applied to spots in a certain area of the skin having been merged in a common individuality, the subject may still think that he can localize the touches. Here he has, as it were, a number of possible places upon which he can localize the touches which seem to him to be similar. One of these may be chosen (perhaps, by "chance"), but thereafter he would be expected to continue to localize all these touches on this one spot of the hand of the model—at any rate, during the course of one series of readings.

In such a case the first localization of a touch which is applied to the affected area may be a matter of chance. Thereafter, all other touches applied to different spots in this area will be referred to the same spot on the model. But if a limited number of spots are taken for examination in the affected area of skin; and if these spots are marked upon the hand of the model; and if the patient knows that the touches of which he is conscious must be localized upon one of these spots on the model or not at all; when the different spots on the patient are touched in an irregular order the patient will either localize the touches all on one of the spots on the model—or will indicate here and there that he is unable to localize a touch. If failures to localize are disregarded, the answers will tend to run in long similar series and (provided each of the spots on the patient is touched the same number of times in the series) the average error will be the same as that of hazard—it will be the same, that is, as if the answers were chosen by lot. The following example from actual experiment is similar to what might be expected to be obtained. Three spots only are examined. The numbers on the upper line are those attached to them; those on the lower line are the numbers of the corresponding spots on the model which were indicated by the patient as corresponding to the location of the touches. The interruptions in the series were not present in the experiment and are here interpolated in order to indicate the series of similar numbers in the answers:—

232	1	3231	3	1	2	3	2112313211	3232313	213212	132312	1
333	1	2222	3	1	2	3	2222222222	3333333	222222	111111	2

Had the answers in the above experiment been determined solely by chance, or had the same answer been given throughout the whole series, the number of wrong answers would have been 28—a percentage error of 66·7. Actually it is 23—a percentage error of 54·8.

In the example given above, it will be observed that, although the answers tend to run in series of similar localizations of dissimilar touches, the same answer is not given constantly. Often, but not always, the first answer in a series is a correct one, and for a time thereafter all the touches are localized on the same spot of the model. It may be that in such a case the attribute of character of the tactile stimuli is not entirely abolished, but is impaired; or it may be that the attribute of individuality is impaired, while the attribute of character is abolished. It is probable that the attribute of individuality attached to tactile stimuli has an element of "memory" in it. If this is defective, it might happen that although the characters of the spots in the affected area of skin are abolished, and the touches which are applied to them seem to the subject to be similar, yet the apparent individuality of the merged character might vary from time to time in the experiment. All the different touches then might at one time be thought by the subject to have the individuality of one of them, and they might be referred by him to the locus of that stimulus; whilst at another time these same different touches might be thought by him to have the individuality of another of them, and would be localized on another position.

If the attribute of individuality is not merely impaired, but is actually abolished along with the destruction of the attribute of character, and if yet the attribute of posture remains, the touches would appear to the subject to be similar, and he would think that he could localize the apparently common touch; but he would be expected to localize it, now here and now there, in the different possible positions. In such a case the error in localization would still be that of hazard; but the answers would no longer tend to run in long similar series.

The following example from actual experiment (in which the test was one of recognition of three different two-dimensional shapes applied to the palm of the hand) is similar to the records which might be expected to be obtained:

312323131212312123213213231321321231312312
332123321223213212321231231231232123313223

Here, out of 42 instances, in which three different stimuli are given each 14 times, 28 wrong answers are given. This gives a percentage error of 66·7 — exactly that which would be expected to be given if the answers had been selected by hazard. But on only five occasions is the same answer given twice consecutively.

Therefore it may be said that if the attribute of character of

touches is lost, but the attributes of individuality and position remain unimpaired, it would be expected that the localization of the different touches would be wrong (the average error being that of hazard); but the different touches would tend to be localized all on the same spot. If, however, the attribute of individuality is lost or impaired along with that of character, it would be expected that the error of localization would be the same as before (that is, the error of hazard), but there would be a tendency to indiscriminate variation in the position to which the touches are referred. If the attribute of position is lost, the patient would be expected to be confused, and unable to localize the stimuli at all.

It is possible to suppose that the attribute of character may be unimpaired, while that of the individuality of the touches is abolished. In such a case one touch will appear to the subject to be different from another, but a touch will not appear to be the same each time it is applied to a certain spot. Therefore if a number of tactile stimuli are applied in an indifferent order to a restricted number of spots on the affected area of the skin, the subject of the experiment will rarely confuse two different successive touches, but he will refer a stimulus which at different times is applied to one and the same spot, now to one of the possible positions, now to another, and only occasionally to the right one. In other words, where the tactile stimuli are not applied twice in succession to the same spot the answers will not tend to run in long similar series; but they will, nevertheless, tend to be wrong, and the average error will be that of hazard. The following example from actual experiment is similar to what might be expected to be obtained in these circumstances:—

231231231321312131292312323131212312123213
321231231233123131313213123131233232131321

Here the number of wrong answers is 23 out of a possible number 42—a percentage error of 54·8. The question “3” is put 14 times, and is given right on 5 occasions and wrong on 9—a percentage error of 64·3. Of the wrong answers “1” is given 5 times, and “2” is given 4 times; so that the percentages of the possible answers — “1” and “2” (wrong) and “3” (right) — are 35·7, 28·6, and 35·7: that is, as near as is possible with a small number of observations to the proportions of hazard. In the case of “1” and “2” in this experiment, this close approximation does not occur.

If the attribute of position of the touches is lost along with that of individuality, the subject would be expected to be unable to make an

attempt at localization, although he might still be able to recognize that there was a difference between touches which were applied to different spots on the affected area.

Finally, if the attribute of position is alone abolished, it is theoretically possible that the subject may be able to recognize differently located touches as in some way different, and a touch as in some way similar to previous touches of the same spot, and yet would still be unable to make a localization of these touches.

We may restate the above paragraphs by saying that for the proper localization of a touch we must probably assume that the sensation conditioned by the stimulus has three attributes apart from its quality. These are—its character, its individuality, and its position. By restricting the number of spots touched in a test, and the number of possible replies of the subject, we have a means of distinguishing between them. If the attribute of position is destroyed the subject should (theoretically) be unable to make a localization, and the error may be termed one of 100 per cent. If the attribute of character is alone destroyed the subject should tend to locate touches which are applied to different spots upon a single spot, so that the answers to series of tactile stimuli, no consecutive two of which are applied to the same spot, should run in series of identical replies. The percentage error should be that of hazard. If the attribute of individuality is alone destroyed the subject should tend to distinguish between consecutive dissimilar touches, but should tend to localize any one individual touch indifferently on any of the possible positions. The percentage error should still be that of hazard, but the answers to a series of dissimilar tactile stimuli, no consecutive two of which are the same, should run in series of which also no consecutive two are similar. If a series of tactile stimuli are applied to the same spot the answers should vary.

It must be noted that, on theoretical grounds, abolition of the attribute of character along with that of individuality should give the same results in the answers to a series of tactile stimuli, no consecutive two of which are the same, as abolition merely of the attribute of individuality. Is it possible to separate these two hypothetical conditions by test?

The investigation of the effects of touching two different spots either synchronously or consecutively with the compasses may possibly give such a test. If the attribute of character is abolished, when the points of the compass are applied simultaneously to two different spots the resultant sensation should, theoretically, be one of singleness. And

singleness should also result when a very short interval of time separates the application of the first point of the compass from that of the second. These effects should also, theoretically, be obtained when the attribute of individuality is lost as well as that of character. If the attribute of individuality alone is lost the simultaneous application of the two compass points should theoretically give a feeling of doubleness, as should also the asynchronous application of the points to two different spots. Thus, on purely theoretical grounds, it is to be supposed that where the attribute of individuality alone is lost the compass tests will differ from those obtained when the attributes of character and individuality are both lost. In the former case there will be no failure to recognize the doubleness of two touches when the compass points are applied either synchronously or successively to two different spots in the affected area; while in the latter case such a failure should occur, and apparent singleness should be the result.

If, as on theoretical grounds seems possible, the localization test serves to distinguish between conditions in which on the one hand the attribute of character only is abolished, and on the other hand either that of individuality alone or those of character and individuality together are lost; and if the compass tests (discrimination of two different tactile stimuli as double whether they are applied simultaneously or successively) serve to distinguish between conditions in which on the one hand either the attribute of character alone is abolished or the attributes of character and individuality are both destroyed, and on the other hand the attribute of individuality alone is lost: then a combination of the two tests should serve to distinguish between the three possible conditions—that in which the attribute of character alone is lost, that in which the attribute of individuality alone is lost, and that in which the attributes both of character and of individuality are lost.

In other words, for the compass test to be a complete one the answer of the subject should not only indicate that there is a "doubleness" about the stimuli, but it should also give data with regard to whether the doubleness is referred to two different spots on the skin or to one and the same spot. When the compass is applied in such a manner that its points fall synchronously upon two different spots and the touches are referred to by the subject as having "doubleness," we may assume that this is referred also to two different spots on the skin. But this is not necessarily the case if the compass points are applied successively with a short interval of time between them (let us say 0.5 sec.).

To meet this problem the following compass tests may be used. They require two compasses, and one arm of one of them is furnished with a small soft pad of leather sufficiently far removed from the point that it cannot come into contact with the skin. Sometimes two different spots are touched successively with a short interval of time between the application of the first and of the second point of the compasses; sometimes a single spot only is touched; and sometimes the point of the compass which is provided with the leather pad is touched on a single spot, and then immediately afterwards an additional touch is applied to the pad of leather by the second compass—the interval between the first and second touch here being the same as that between the application of the first and second point of the compass when two different spots are touched successively. The subject states that the touch is a double one applied to two different spots; that it is a single one; or that it is a double one applied to the same spot. In the second test sometimes one point of a compass is applied to a single spot; sometimes the two points of the compass are applied successively to two different spots; and sometimes two compass points (one of each compass) are applied successively very close together to almost the same spot. The subject again gives one of the three above answers.

The normal subject can distinguish between the different elements of these compass tests. If, however, the attribute of character is lost (without the abolition of the other attributes and without any other disturbance) the subject will, theoretically, be unable to distinguish between the successive touching of two different spots and the successive touching of nearly the same spot with the points of two different compasses. In both cases, theoretically, he may recognize the touches as double; but the synchronous touching of two different spots will seem to him to be single. Where the attribute of individuality is lost alone the subject should theoretically be able to distinguish correctly between the two points applied synchronously to two different spots; the two points applied successively to the two different spots; the points of two different compasses applied successively to nearly the same spot; and of course the single compass point applied to one spot. If the attributes both of character and of individuality are lost the results of the tests should theoretically be the same as in the case of loss of character only.

With loss of the attribute of position alone (without loss of the other attributes) normal results should theoretically be given to the different compass tests even when the patient is unable to make the attempt at localization.

In these theoretical considerations we have of course made the assumption that it is possible that one only of the attributes of the tactile sensation may be lost, or that one may escape from a destruction which overtakes the other two. If such a dissociation between destruction of the different attributes does not occur—that is to say, if they are so closely bound together that if one is destroyed or impaired the others are also destroyed or impaired—it is clear that no tests will serve to distinguish between them. Then the effects of all cortical lesions which destroy or impair the faculty of localization of tactile stimuli will give similar results—which may, indeed, differ in degree, but will not differ in kind.

It is interesting here to note the observations of Head and Holmes [1] on this point. They state that “in a certain proportion of cortical cases it does not matter whether the compasses are applied simultaneously, or whether an interval is allowed to elapse before the second point touches the skin. The power of recognizing the double nature of the stimulus is lost and no increase of the distance between the two points makes a constant or material difference to the accuracy of the answers. . . . Evidently he (the patient) has lost that faculty by which ‘two-ness’ is recognized, and it does not matter whether the points are applied simultaneously or successively. Now, whenever successive application of the two points is recognized, localization will be found to be intact. The power of appreciating two points applied successively is in reality the faculty of localizing two spots that have been stimulated one after the other. It is independent of the power of discriminating two stimuli which act upon the surface at the same moment.” To this question we shall return in parts of this paper to be published later.

In this analysis of the faculties of localization and discrimination of tactile stimuli we have so far confined ourselves to what may be termed “negative” error. It is clear that there may be a difference between possible errors of localization in which the subject, even although he thinks his localization in each case to be correct, places a specific touch, now here and now there, indifferently upon the different positions in a restricted test, and possible errors of localization in which the subject constantly places a specific touch upon the same wrong position. Let us suppose that the test for accuracy of localization is one in which a small number of different spots is used, and that the tactile stimuli applied to them are given in an indifferent order in which no two consecutive stimuli are applied to the same spot. In the former case the

total average error of localization will be that of hazard, and if the answers to any one specific stimulus are examined it will be found that they vary amongst the possible answers—the individual average error of the answers to that stimulus still being that of hazard. But in the latter case the total average error might even be as high as 100 per cent., as might also be the individual average error of localization for each specific tactile stimulus used in the test. Thus let us suppose that three spots only are chosen for examination, and that the subject knows that there are three possible answers in the case of each tactile stimulus—only one of the answers being correct, that is, corresponding accurately to the locus of the stimulus. In the former case the subject will call stimulus “3” indifferently “1,” “2,” or “3”; and in a sufficiently large number of answers 33·3 per cent. will be given to each kind. That is to say, that of the whole series of answers 33·3 per cent. will be right; 66·7 per cent. will be wrong, and the wrong answers to each of the three stimuli will be equally divided between the two possibilities. But in the latter case the subject may always localize stimulus “1” at “2,” stimulus “2” at “3,” and stimulus “3” at “1.” The average error will here be 100 per cent. for the whole series, and 100 per cent. for the answers to each specific stimulus, while the wrong answers to any one of the three stimuli will not be equally divided between the two possibilities.

In a case in which there is persistently a greater error than that of hazard it is clear that something more than the mere abolition of the faculty of localization (or of one of its factors) is present. There must be an actual distortion of it—an actual constant error, not an indifferent error. This error we may term a “positive” one.

On theoretical grounds we may assume for the moment that our hypothetical attribute of position may either be abolished or distorted by a cortical lesion. In the former case there should be no localization of a touch, even although its attributes of character and individuality are unimpaired. In the latter case localization may be present in these circumstances, but it may be inaccurate. That is to say, that the localization of a certain touch which has the attributes of character and individuality, but has a wrong attribute of position, may be done in an inaccurate manner, but the error will always be the same.

The method of testing localization for a restricted number of spots may bring out this type of error if it really occurs. The test in which the number of spots touched is not limited can hardly be expected to

do so, for there the error of hazard is about 100 per cent.; in such a case the only indication of this type of error is the personal opinion of the investigator that a certain tactile stimulus is always referred to a certain wrong position on the model. Records in which the number of different tactile stimuli are limited, as also are the possible answers, will give an error of hazard which is appreciably less than 100 per cent. (i.e., 66·7 per cent. where three different stimuli are used, 75 per cent. where four are used, and so on). If the average error in such records is constantly and appreciably greater than the error of hazard it may be inferred that the error is a "positive" one and not a "negative" one—to use the terms in the sense which we have already given to them. If such a record is analysed still further and the average individual error of localization for each tactile stimulus is obtained it may be found that these errors differ. Thus it might be that the total average error in the answers to the whole series of different stimuli is in fact about that of hazard, but that the individual average error in the answers to the stimuli which are applied to one of the spots is markedly greater than the error of hazard. A further analysis might indicate that in the case of the answers to this stimulus there is a preponderance of one specific wrong answer, and that the wrong answers to it are not evenly divided amongst the possible wrong answers

The following example from actual experiment brings out this point. It actually is a record of the answers to three different two-dimensional stimuli—flat objects of three different shapes applied to the palm of the affected hand:—

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123231312321312132321213213232123132312123
13232121322131212312131221111112123223112
212313123123231213123123231212312132132313
3332222322331131222222222312111212112211
```

In this example the number of wrong answers is 51 out of a total of 84 answers—an average error of about 60·7 per cent., the error of hazard being 66·7 per cent. The individual average error in the answers to "1" is about 35·7 per cent.; that for "2" is about 57·1 per cent.—smaller than the error of hazard; and that for "3" is about 89·3 per cent.—much greater than the hazard error. Each of the three different stimuli is given 28 times, and when the wrong answers to "2" are analysed it is found that "2" was called "1" 5 times, and was called "3" 11 times—there, therefore, being a marked disposition to call "2" "3" when it is wrongly named. Of the wrong answers to "3," 8 are called "1," and 17 are called "2." In this

case there, therefore, seems a definite confusion of the stimulus "2" with the stimulus "3" and the error is too great to be due to hazard. As a matter of fact the individual average error per cent. in the answers to the stimulus "3" on six consecutive days was 75, 85.7, 89.3, 82.1, 78.6, and 71.4—in each case above, and sometimes markedly above, the error of hazard, which here was 66.7 per cent.

What may be supposed to happen in our so-called "positive" error of localization is that the spot indicated by the subject as corresponding to the position of the touch which he perceives lies in some constant relation to the true corresponding position. As Head and Holmes point out, Russell and Horsley [1] state that this is the case in disturbances of localization by cortical lesions. The former observers, however, believe that their own failure to discover such a uniform tendency to erroneous localization is due to the avoidance of the "groping" method of testing localization—the method in which the subject (not seeing the spot stimulated) tries to touch with his other hand the spot to which the tactile stimulus has just been applied—and to the elimination of error due to defective recognition of the posture of his limb by the patient. They say, "We cannot insist too strongly that, when localization is defective from lesions of the cortex, the stimulus is not localized in some false direction, but the patient has a vague and uncertain idea amounting in some cases to complete ignorance of its position."

Another point in connection with our hypothetical attributes of character, individuality, and position may be noticed. The attribute of position has obviously attached to it (or has as a part of it) permanent memory. It is the relating of a tactile sensation, the character and individuality of which are presupposed, to a certain part or point in the subject's "schema" (to use Head's term) of the surface of his body. For the accuracy and constancy of the attribute of position of touches applied at different times to the same spot of the skin permanent memory would seem to be necessary. In a similar manner permanent memory would seem necessarily associated with the attribute of individuality—perhaps the two attributes are closely connected, at any rate as regards this permanent memory. But is permanent memory of necessity connected with the attribute of character?

Theoretically, at any rate, it is possible to suppose that this sort of permanent memory is not necessarily attached to the attribute of character. Thus it may be conceded that tactile stimuli applied to different spots on the skin condition activities in the cortical mechanism which are in some manner different. The parallel changes in

consciousness which accompany these changes in activity may also be different, and in short, the sensations conditioned by the different stimuli are recognized in consciousness to be different—if they are present in consciousness at the same time, and can thus immediately be compared the one with the other. But if the different stimuli are not applied synchronously it would at first sight appear that an element of memory is necessary for the bringing together of the sensations which they subtend and for their comparison in consciousness. This is, perhaps, not necessarily so.

If the sensations conditioned by tactile stimuli were of infinitely short duration in consciousness, the comparison of two asynchronously applied stimuli would appear to be inconceivable without a link of memory. But it is probable that the sensation conditioned by a tactile stimulus has a definite duration in consciousness—there is a sort of “after-discharge.” One of us has shown that electrical stimulation of a point in the “motor” area of the cortex cerebri is followed by a state of facilitation during which the point remains more excitable than usual to the electrical stimulus; and that the duration of this state—which is probably that of the “facilitation” which has been postulated for cortical “motor” (and also “sensory”) activities—is a comparatively short one, 10 min. to 20 min. for liminal stimuli. Now, if we suppose that the activity which underlies the sensation in consciousness of a tactile stimulus may persist, slowly dying, after the withdrawal of a stimulus, and if this continuance of activity is paralleled by a persistence of the change of consciousness, another stimulus applied to a different spot during the continuation of the “sensory after-discharge” would be paralleled by a change in consciousness which would synchronize with the dying after-effect of the first. In a manner the two sensations would be present synchronously for comparison in consciousness. But it must be noted here that the dying after-effect of the sensation in consciousness may well be likened to a sort of transient memory; and that the after-discharge and dying state of facilitation of the physiological mechanism (“motor”) might in a sense be regarded as the physical counterpart of such transient memory. It is not, perhaps, altogether unwarranted to apply this idea of facilitation to the “sensory” mechanism, for it seems to be present in the mechanisms of the post-central convolutions which are usually looked upon as “sensory” in function.

This state of “facilitation” may possibly be one of the physiological factors which underlie the psychical attribute of “character” in the

sensations conditioned by tactile stimuli. The recognition of different touches simply as different apart from the recognition of their locus may be conditioned in part on the physiological side by the state of facilitation of the mechanism. Thus a second stimulus applied sufficiently soon after a first to the same receptors should give a greater response; stimuli of different intensity applied at different times to the same receptors are recognized to differ; if now stimuli of the same intensity are used and this is within the knowledge of the subject, stimuli applied sufficiently close together in time to different spots may be recognized as different. For if two stimuli of equal intensity are applied soon one after the other to the same spot the sensation conditioned by the second will appear to be more intense than that conditioned by the first. If two equal stimuli are applied one after the other and the sensations conditioned by them do not appear to the subject to be different in intensity, he may infer that the stimuli have been applied to different spots. This is, perhaps, too far-fetched, and at any rate such a factor could not be the sole condition of difference in character of touches, for it would be hard to explain by it the recognition of doubleness of contact when two different spots are touched simultaneously.

Before concluding this section of the paper we cannot refrain from a speculation which we think may lead into interesting paths of investigation.

The psychical process of the localization of sensations is, as it were, a process of apprehension, and this seems to be conditioned by three chief sets of factors—the sets of factors associated respectively with the “character,” “individuality,” and “position” of the sensation.

But the process of apprehension is associated with other than the more or less simple sensations which are conditioned by what for practical purposes may be regarded as one-dimensional tactile stimuli; that process is also associated with the compound tactile (and deep pressure) sensations which the stimuli engendered by two-dimensional objects condition—and with the compound tactile, deep pressure, and kinæsthetic sensations conditioned by the stimuli which three-dimensional objects engender.

And, again, the process of apprehension is not restricted to the sensations conditioned by the activities of the sense organs of the skin, subcutaneous tissues, muscles, tendons, and joints; it is thus also associated with the sensations conditioned by the activities of such organs of special sense as the retina and the cochlea.

The interesting question therefore arises whether these other processes (which are in some manner, perhaps, comparable to the process of localization) may be analysed in terms of the three same sets of factors—character, individuality, and position.

In the case of the apprehension of the sensations conditioned by two-dimensional objects pressed upon the skin we have already satisfied ourselves that this obtains; and we have a little evidence which suggests that the process of apprehension of printed words and letters may also be analysed in terms of these factors.

Thus, for the proper description by the subject of flat objects of different shapes (of which he is allowed to be aware only through the sense organs of the skin and subcutaneous tissues), he must be aware of the character of each object—its difference with regard to the others, the individuality; its sameness each time it is pressed upon the skin; and the position—that is, its relation to one of his “schemata.” It must be noted here that in the process of localization the factor of “position” refers not at all to the place upon the body to which the stimulus has been applied, but to the place of the sensation within the subject’s schema of the surface of the body. In this sense the word may also be used to denote one of the factors (or sets of factors) in the process of apprehension of two-dimensional objects; that is, it may be used to express the place of a certain two-dimensional object within the subject’s schema of such things.

The heard or seen word is apprehended and recognized, and in the process of recognition there may, perhaps, be discerned the same three sets of factors. Thus, a certain word must in the first place be recognized as different from all others—there must be factors of character in the recognition of words; and it must be recognized as similar to itself each time it conditions sensations (either visual or auditory)—it must have individuality; while, finally, it must be related to the subject’s schema of words—it must have position. With the written or printed letter or the unitary sounds in heard speech these three factors may, perhaps, be relatively simple; but with the heard or seen word they are obviously much more complex. This complexity is increased by the fact that certain similar words may have different “positions”; thus the printed word “smack” has its factors of character and individuality but many positions. Its meanings are various: “a small ship, a loud kiss, a sharp noise, a smart blow, a taste, a tincture, a small quantity,” and so on—to take only its meanings as a substantive. Here the positions of the word in its recognition are probably a factor conditioned

not only by the seen word itself but by the context—its environment or “background.” [It would, perhaps, be more correct to say that many different words have the same character and individuality, than to say that a certain word has many different positions.] In a similar manner heard words may have similar characters and individualities but different positions—such an example as “sow,” “sew,” is sufficient to demonstrate this.

Quite another form of complexity lies in the fact that words which have different characters and individualities may have the same position. Thus “gauge” and “measure” may have identically the same meaning. It is interesting to note that, in the case of two words which have many meanings, but only one common to both, the effect of the context is a predominant factor in the conditioning of the position.

Of course the schema of language is very much more complex than the schema of the loci of cutaneous sensations, but we suggest that there is much similarity between the two. The position of a word in the language schema (or schemata) may be related to all which we denote when we talk of the meaning of a word; but it must be observed that a single word may be related to many different schemata, each of which forms a part of the complex which we may term the schema of heard and seen language. The position of a word may be common to many schemata; and we may make a simple model of the relation between the position of a word and the different schemata to which it is related by figuring the schemata as geometrical planes, and the position of the word as a geometrical point. We may then figure the relation between a word and its schemata by supposing that the different planes intersect each other at a single point—the position of the word.

In the case of language the position of a word is common to at least two sensory complexes—the seen word and the heard word. Indeed, it must be common to more than these two, for the position of a word in the process of recognition must be common to the different forms in which the seen word may be presented (that is, the written word and its different forms, the printed word and its different forms, the word written or printed in different colours of ink, the word as recognized by touch, the word as written or printed in different alphabets; for instance, in shorthand or in the raised characters of the Braille system of printing for the blind—the corresponding word in various different languages, and so on).

The subject's schemata of different classes of sensations seem probably to be (as it were) catalogues of common elements in many different sensations. This is, perhaps, peculiarly so in the case of the language schemata, but it must not be forgotten that it also obtains in so comparatively simple a schema as that in which the cutaneous sensations are related together in the process of localization. Thus the sensations conditioned by tactile stimuli, by stimuli of heat and of cold, and by pain stimuli, all of which are applied to a given small area of the skin, are referred to a common locus in the process of localization. That is to say, that these sensations have a common factor of position in their localization. In other words, each of them is referred to the same part of the subject's schema of the surface of his body.

We would like to suggest that the method of experiment used in this investigation is eminently adapted for the proper examination of these different subjective schemata, and for the analysis of the factors in the apprehension of sensory complexes—either the relatively simple process of localization (which seems capable of analysis in terms of three or more sets of factors) or the relatively complex process of apprehension of heard and seen language.

That method—which we believe to be a new one—necessitates a subject in which there is some disorder of the process which is to be investigated. Given this condition, the method consists in the restriction of the number of different stimuli presented to the subject (be they tactile stimuli, the stimuli conditioned by two-dimensional objects, auditory stimuli, visual stimuli, and so on), and in a restriction the number of answers which the subject is allowed to give. This restriction of the answers is obtained by allowing the subject to know the number and the different forms of the stimuli which are to be presented to him, but not the order in which they will be given. Accurate records of the answers (whether they be right or wrong; and, if wrong, the nature of the reply) are taken, and are then finally analysed after a correct estimation of the percentage error of hazard. The answers to the stimuli are scrutinized in the first place with reference to their order in series. Attention is paid to the possible error of giving the same reply consecutively to consecutive stimuli of different sorts—this type of error denoting defect in the factor of character—and to the possible error of giving different consecutive replies to consecutive stimuli of the same sort—this type of error denoting defect in the factor of individuality. In the second place the replies to each individual sort of stimulus are scrutinized after determination of the

hazard proportion of each possible answer to the sort of stimulus which is being analysed. A reply which is given in a greater proportion of times than the hazard proportion may be termed a positive one, and where the reply is incorrect it may then be termed a positive error. The occurrence of positive error seems definitely to point to a distortion of the position factor in the apprehension of the sensation conditioned by the stimulus which is being analysed.

This method of investigation, which may be suggested as one suitable for use in all cases of disturbance of the process of apprehension, may be termed the method of restricted test analysed in terms of positive error by reference to the error of hazard.

III.—METHODS EMPLOYED.

(1) *The Subject of the Experiment.*

J. H. L., born in 1886, wounded on October 26, 1914, by a rifle bullet through the left side of the head.

The wound of entry is represented by a small round hole in the skull, and about 1.5 cm. in diameter. Its nearest point to the central line lies about 5 cm. from it (on the left side of the skull), and the distance between the nasion and that point on the central line of the surface of the head which is cut at right angles by a line passing through this wound is about 12 cm.

In a similar manner the wound of exit lies (at right angles to the central line) 3 cm. to the left, a point on the central line—the distance between the nasion and that point being about 29 cm.

There is a trephine opening in front of the wound of exit. Its longest axis is parallel to the central line of the head, and is about 7 cm. long. Its most anterior point lies about 3 cm. to the left of a point on the central line which is about 22 cm. posterior to the nasion; its breadth is about 4 cm.

A description of the case is given in a later section of this paper. The experiment was begun on January 7, 1916, more than fourteen months after the infliction of the wound.

(2) *Methods of Examination.*

In this experiment the accuracy of the subject's localization of tactile stimuli of different intensities, of painful stimuli, and of stimuli of heat and of cold, was registered at different times. So, too, was the

accuracy of his responses (as regards doubleness or singleness) in the compass test, and the accuracy of his recognition of three differently shaped flat objects of indifferent temperature placed in contact with the surface of the palm.

In testing the accuracy of localization of tactile or other stimuli, we made use of the Henri method as modified by Head and Holmes. Stimuli were applied either to the dorsal or to the palmar aspect of the hands (the right hand being that which was affected), the arm first being passed through the opening of a screen which prevented the subject from seeing the spots which were touched. A model held his corresponding hand in the same posture as that of the subject. This hand was within the subject's field of vision, and he indicated upon it with a pointer (held in the other hand) the position which he thought to correspond to the location of a tactile stimulus which had just been applied to his own hand. The normal hand was withdrawn from behind the screen (in order to indicate the localization when control observations were made upon it).

For the purposes of our experiment, and for ease of registration, we restricted the loci of the stimuli to nine different specific spots on each of the second, third, fourth, and fifth digits of either hand. Of these nine spots, in each case three were situated on the dorsal aspect of the finger (see fig. 1), and were so placed that a spot lay on the skin about midway between the two extremities of each of the three phalanges. In the case of each finger six different spots were situated upon the palmar aspect. Three of these spots were placed, as in the case of those on the dorsal aspect, one about midway between the two extremities of each of the phalanges (see fig. 2); the remaining three spots (see also fig. 2) were placed on the folds of the skin near the metacarpal-phalangeal, and the two inter-phalangeal joints respectively—that is to say, about midway between pairs of the other spots. All the spots lay upon that dorso-ventral plane which passed through the long axis of the finger.

This gave us three sets of three different spots each, and we numbered the different spots in each set "1," "2," and "3" in their order from the extremity of the limb towards the trunk. The spots were permanently marked with silver nitrate; and spots corresponding to them were marked upon the fingers of the model.

In an experiment a stimulus was applied to a certain spot and the subject then (a) failed to give any response (this failure being recorded), or (b) tapped the end of his pointer upon the table to indicate that he



FIG. 1.—Photograph of the dorsal aspect of the subject's right hand. The three spots on each finger ("dorsal sets of spots") are shown, having been marked with ordinary ink for the purpose of the photograph.



FIG. 2.—Photograph of the palmar aspect of the subject's right hand. The six spots on each finger ("ordinary" and "untrained" sets) are shown with the exception of the distal spots (spots "1" of the "ordinary sets") on the index and ring fingers, which are covered by the observer's finger-tips. On the middle finger the spots from left to right (that is, distal to proximal) are "spot 1" ("ordinary set"); "spot 1" ("untrained set"); "spot 2" ("ordinary"); "spot 2" ("untrained"); "spot 3" ("ordinary"); "spot 3" ("untrained"). The black patch on the palm was the mark used in training experiments on discrimination of two-dimensional objects not here described.

was unable to make a localization of the touch which he yet perceived, or (c) touched with his pointer the marked spot upon the model which he thought corresponded in position with that to which the tactile stimulus was applied upon his own hand. If no localization was made (although the subject was aware of the stimulus) a mark was placed upon the record under the corresponding number of the spot which was stimulated, and that stimulus was not repeated. When no response was given—the touch not being perceived—the stimulus was repeated. If a localization was made the corresponding number which we attached to the spot indicated on the model was written below the number of the spot touched on the subject. “Dilemma” could usually be detected by observing the movements of the pointer, and when it occurred was registered on the records. The examination was conducted in silence, and throughout the whole duration of the experiment the subject was never allowed to see a record, nor on any occasion was he allowed to know whether his reply had been right or wrong. Owing to the slight contracture of the affected fingers one of the observers held the finger that was being examined in a posture of extension.

In the first part of the experiment we gave the stimuli to the different spots in a series, the order of the elements of which (“1,” “2,” and “3”) was selected by lot. In consequence of this there were slightly unequal numbers of the three different spots in a series, and sometimes a certain spot would occur several times in immediate succession. In the succeeding parts of the experiment (not here published), we used a new set of records in which, while the order of the spots was selected by lot, no two consecutive ones were the same and in which equal numbers of each spot were present in each record.

We usually examined the accuracy of localization of touches for one of the sets of three spots on each of the fingers separately—the subject being allowed to know which finger was being touched in any one test. At first we used records in which twenty-five consecutive tactile stimuli were applied to the three different spots (an average of about 8·3 stimuli to each spot). Later we increased the number of stimuli in a series to forty-two, of which exactly fourteen were applied to each of the three spots.

The stimuli were applied at the rate of about one every five seconds, and intervals of one minute each were allowed to elapse between the series of stimuli which were applied to different sets of spots.

The sets of spots on the different fingers were examined in a constant order in the ordinary daily tests. First, two palmar sets—one on each

of the third and fourth digits of the normal left hand. Then a palmar set on the second, third, fourth, and fifth right digits in that order. Then the dorsal sets of spots on these six fingers in the same order as before. Finally, for purposes of control, the palmar set of spots on one of the normal fingers was again examined, and occasionally the palmar set of spots on the second right digit.

For purposes of control, and to obtain additional data, from time to time we did this test without allowing the subject to know which finger was being touched, but allowed him to know the position of the twelve spots which were to be touched upon the four fingers. In this test (as a rule) no one finger was touched twice consecutively, and the order in which the fingers were touched was otherwise selected by lot—equal numbers of stimuli, however, being applied to each finger in the test. In this test usually 84 stimuli were applied (sometimes 168) in consecutive series of 21 each, with intervals of one minute between the series.

The tactile stimuli used were given by pressing hairs, each of which exerted a constant pressure when force sufficient to bend it was employed (the hairs were of different stiffnesses in different tests) on the selected spots; painful stimuli by stabbing the spot with the point of a needle; heat and cold by applying a hot or cold flat metal surface (*circa* 5 mm. in diameter) so gently against the spot that it gave the least possible recognizable sensation of touch. We also on one occasion gave tactile stimuli by pressing the open end of the cap of a fountain-pen against the skin in such a manner that it encircled, but did not touch, the spots used in the other experiments. In the first series of records we used as a constant stimulus on consecutive days a hair of stiffness just insufficient to give a painful sensation when applied to a spot on the normal palm; in the following series of experiments we used a small apparatus for giving constant pressure-touch stimuli. This, which we made ourselves, consisted in a rod (the end being a bad conductor of heat) which worked in a hollow holder against an elastic band.

The normal error of localization of tactile stimuli applied with these instruments which we used in the day to day tests is, in the normal subject, about 0.0 per cent. on the palmar aspect when the test is restricted to a single finger. When it is not so restricted to a single finger, but when the possible spots on each finger are restricted to three, the normal error for the palmar aspect of the fingers seems to be about 8 per cent. The tactile stimuli are rarely localized on the

wrong finger (when they are the finger touched is usually the third or fourth digit, and the stimulus is referred to the fourth or third) and the error usually consists in wrongly placing a stimulus upon the right finger. The spot thus wrongly localized is usually "spot 3"—i.e., that of the three nearest to the trunk, less often "2," and seldom or never "1"—that situated on the pulp of the terminal phalanx. The error is usually made by localizing "3" on "2"; less often by localizing "2" on "3"; seldom or never by localizing either "2" or "3" upon "1." We have never, on our own persons, seen an error in which a tactile stimulus delivered with these instruments was localized wrongly both in regard to the finger and to the position of the spot on the finger.

(3) *The Method of Training used in the Experiment.*

The general aim which we had before us was the investigation of the possibility that a lost "sensory" function, probably of the cerebral cortex, can be regained—just as recovery of "voluntary" movement may occur in monkeys and higher apes after a cortical lesion of the so-called "motor" area. Although such a recovery of a lost "sensory" function has not yet been observed to occur "spontaneously," it is possible that it might do so under the influence of training. Tests of the accuracy of localization, &c., of tactile stimuli before and after such an attempt at training may yield evidence as to its effects.

In applying the training a single finger was selected and it only was trained at that time. Not only this. The training was applied only to one of the three sets of three spots on that finger—the other two sets remaining untrained. The three spots which were trained were, in every case, those situated about the middle points of the pads of the fingers which lie over the middle of the palmar aspects of the three phalanges.

In this manner we were able to compare the accuracy of localization of stimuli applied to the "trained" spots after the training with that of corresponding but untrained spots on the other fingers; with that of the untrained spots on the back of the trained finger; and with that of untrained spots on the palmar aspect of the trained finger (these untrained spots lying on the folds in the skin near the metacarpal-phalangeal and the two interphalangeal joints).

The training was performed in the following manner: An ordinary localization test having been done for the spots which were to be trained, the subject was allowed a short interval of rest. Then he was told

that spot "1" was going to be touched and that he was to concentrate as much as possible upon his experiences during the stimulation—trying to realize the peculiarities of the stimulus, &c. That spot was then slowly stimulated 10 or 20 times in succession with the ordinary instrument—and he was allowed to see each alternate touch being given by the silent removal of the screen. In the same way 10 (or 20) successive touches were applied to each of the other spots—"2" and "3." After a short interval of rest the subject was allowed to look at his finger while 50 successive touches were applied in an indifferent order to the three different spots. Then, after another interval of rest, the ordinary test of the accuracy of localization of tactile stimuli on these same three spots was again done—the subject now not being allowed to see his hand, and having to point to the corresponding spots on the hand of the model. During the training the subject was at one time told to concentrate his mind especially upon the similarity of the stimuli which were then being applied consecutively to the same spot. At another time he was told to concentrate upon the dissimilarities of stimuli which were being applied consecutively to different spots.

This training was usually done in the evenings of a series of consecutive days; sometimes it was performed repeatedly (at two-hour intervals) on the same day. During and after a period of training the ordinary tests were applied in the morning.

(4) *The Course of the Experiments.*

In our first series of tests, on 13 consecutive days we investigated the accuracy to localization of the spots on the palmar and dorsal aspects of each finger of the right (affected) hand of the subject, as well as the corresponding spots on the palmar and dorsal aspects of two of the fingers of the left hand. The stimulus used was the same throughout—that given by pressing a hair against the spot (the hair being a fairly stiff one, but not one which gave a painful stimulus on the normal hand). In addition we used the test in which the stimulus was applied to spots on any of the fingers.

On the fifth, sixth, and seventh days of the series the three palmar spots of the right index finger were trained. The accuracy of localization for tactile stimuli before the training was on this finger intermediate between that of the most defective and that of the least defective finger—but nearer to the former than to the latter. On the seventh day of the series the accuracy of localization on the right index finger was tested (after the training in the morning) every hour from 11 o'clock

in the morning to 9 o'clock at night. Thereafter the tests were continued as before; but on the ninth day of the series the accuracy of localization on the right index finger was tested thrice during the day at four-hour intervals; on the tenth day of the series it was tested four times during the day at three-hour intervals; and on the twelfth day of the series it was tested seventeen times during the day at half-hour intervals. In addition to this, on the tenth, twelfth and thirteenth days of the series the accuracy of localization of tactile stimuli was tested for the set of three untrained spots on the palmar aspect of the index finger (that is, the spots situated near the three joints)—and for the corresponding spots on the other fingers. While on the thirteenth day of the series the training of the spots of the palmar aspect of the right index finger was performed again, on this occasion the training being done four times during the day at two-hour intervals.

On the fifteenth day of the test (three days after the fourteenth) we asked one of our colleagues (Dr. W. H. R. Rivers) to make an examination of the affected hand before making him aware of the nature of our experiments. He came to the conclusion that there were gross errors of localization of tactile stimuli which were applied to the palmar and dorsal aspects of the right hand.

IV.—ON THE CONCLUSIONS WHICH MAY BE DRAWN FROM THE FIRST PART OF THIS EXPERIMENT.

For the easier reading of this paper, we think it best to give here the conclusions which, we believe, may legitimately be drawn from the results obtained in that part of the experiment with which we are dealing—reserving the more detailed analysis of this part of the experiment to the following section of the paper.

It must be clearly understood in the first place that we have no definite knowledge of the situation, nor of the extent, of the cerebral injury—save only that in part that injury is situated in the parietal lobe of the left cerebral hemisphere. We have also no definite knowledge of any changes which may have taken place in the cerebrum during the course of the experiment, but we think that, as we started the experiment fourteen months after the infliction of the wound, any possible process of recovery should by that time have ceased.

The part of the experiment which we consider here is a small portion of the whole. We give the facts as they were; and our conclu-

sions are drawn only from the facts here given, and they are drawn irrespective of the facts obtained later in the experiment—save only that we know that a similar improvement of the accuracy of localization of tactile stimuli occurred when we selected another finger for training.

Now with regard to the state of the subject at the commencement of the experiment:—

The man was unable accurately to localize tactile stimuli which were applied (amongst other places) to the palm of the right hand and to the palmar aspects of the right fingers; the defect of localization was, in fact, gross. He was not, however, unable to attempt a localization. In fact, when a spot in that region was touched, the subject usually made a localization—even although that localization was often a wrong one. He, occasionally, was unable to make the localization at all when the test was limited to a certain small number of spots, but this inability lasted only for the first eight days of the experiment and the stimuli which he was unable to localize were only about 10 per cent. of the whole. Dilemma in the reactions of localization also occurred, but this also decreased as the experiment proceeded. Neither dilemma nor confusion occurred when the test was an unrestricted one—that is, the ordinary clinical method.

A striking characteristic in some of the cases cited by Head and Holmes was that the subject was frequently unable to make the localizations of tactile stimuli. In the present case there is no such inability—but a large proportion of incorrect localizations is made. Recently, we have had the good fortune to be able to investigate another similar case. In this second instance the error of localization is very large; but there is an almost complete absence of dilemma, and the proportion of instances in which localization cannot be made is small. In this second case a remarkable feature is the apparent certainty with which the subject makes the localizations. So great was this, that at first we suspected that he was making them by hazard. But the records show that this probably is not the case. We may conclude that in the subject of the experiments here described the effect of the lesion has not been to wipe out the function of localization of tactile stimuli for a certain part of the body, but only to destroy or to distort certain elements in the complete function.

In the complete process of localization of tactile stimuli we may distinguish three elements or attributes (as regards localization) of the sensation conditioned by each stimulus. These are: (1) the element of “character” (whereby the sensations conditioned by differently located

tactile stimuli are recognized as in some manner different from each other); (2) the element of "individuality" (whereby the sensations conditioned by tactile stimuli which are applied at different times to the same spot on the skin are recognized in some manner to be similar to each other); and (3) the element of "position" (whereby the sensation conditioned by a certain tactile stimulus is recognized as in some manner connected with a definite point in the subject's schema of the surface of his body). As in this experiment the spots which were touched lay upon the fingers of the right hand we may recognize at least two factors in the element of position. The first of these is the place of the touched spot upon the finger. But as there were four fingers all very much alike—that is, four different possible places for each spot—there must be a factor of "finger" in the position of the spot, a factor whereby the subject recognizes that in some manner the tactile stimulus has been applied to a spot on a certain finger. The elements of character and individuality are possibly more fundamental than the elements of position. The latter, perhaps, are those which relate the sensation conditioned by a specific tactile stimulus (with its character and its individuality) to the schema of the surface of the body.

As it is obvious that if the element of "position" in the localization of tactile stimuli is destroyed, the subject should be unable to make any localization of them, and as in this experiment such localizations were made (although often incorrectly), we may conclude that at any rate the element of position was not abolished. But it is yet possible that in our case the elements of position were distorted, although not eliminated. Our results definitely point to this conclusion.

Thus, in the first place, the error of localizing stimuli, which were applied to certain of our chosen spots, was greater than the error of hazard. Such an error may be termed (for our purposes) a "positive" one; and its occurrence clearly indicates that in these instances there was not a mere elimination of an element in localization, but a distortion of it. Thus the tactile stimuli, which were applied to a certain spot (e.g., spot "3") on a certain finger might be definitely thought by the subject to have been applied to another spot (e.g., "2") upon the same finger; and every time (or nearly every time) a tactile stimulus was applied to that first spot, it might be localized by the subject upon the second. In such a case what is at fault is the factor of "place," or "position," within a certain schematic field, of the sensation conditioned by the tactile stimulus, and the error is a definite one.

In the second place, the error of localizing a touch upon the correct

finger (that is, within the correct cutaneous field) was in some cases greater than the error of hazard. This shows that here also there was no mere partial elimination of a factor in the element of position, but a definite distortion of that factor. The subject definitely thought that a large proportion of the tactile stimuli which were applied to spots on a certain finger were applied to spots on a certain other finger.

It is quite possible that such distortions of the elements of position in the localization of tactile stimuli might be sufficient to account for the badness of localization in such cases as that under consideration, even if the elements of character and individuality in the tactile stimuli were perfect. But in this case distortion of the elements of position can hardly have been the sole condition of the badness of localization.

Thus the subject at first repeatedly failed to recognize the differences between differently located tactile stimuli, which were applied in a consecutive series. Thus he might make the same localization—give the same answer—to each of a long series of tactile stimuli, no consecutive two of which were applied to the same spot. This definitely shows that one of the conditions of the badness of his localization of tactile stimuli was the failure to recognize differently located stimuli as in some manner different; in other words, the element of character in the localization of the tactile stimuli was at fault.

Again, the subject at first repeatedly failed to recognize the similarity between the elements of consecutive series of tactile stimuli which were applied to the same spot. Thus at times he would localize series of similar stimuli upon different spots, no consecutive two of which were the same. Here the element of individuality in the localization of tactile stimuli is at fault; the subject is unable to localize correctly a certain specific stimulus, but his error is not a constant one; when this stimulus is repeated in consecutive series, he localizes it now here, now there.

Thus the disturbance of localization of tactile stimuli in this case was probably a mixed one as regards the different elements in that localization. In the first place there was a definite defect in the elements of character and individuality in the localization of tactile stimuli; and in the second place there was a defect, amounting in some cases to positive error, in the element of position.

Such being the condition of the subject, we set ourselves to train selected spots upon the palmar aspect of one of the fingers. The training was directed to improve the elements of character and individuality of the spots, and to improve the factor of "place on the

finger" in their positions: but no direct attempt was made to improve the factor of "finger" in their positions, nor to improve the elements in the localization of any of the spots on the other fingers.

The result of this training was twofold. In the first place there was a very marked improvement of the localization of tactile stimuli on the trained spots both as compared with the accuracy of that localization on the same finger before the training, and with the accuracy of localization upon the other fingers after the training. In the second place there was a much smaller general improvement of the accuracy of localization on the other fingers as compared with their individual accuracies in the records which were taken before the training of the right index finger was commenced.

Of the three spots which were trained upon this finger, one showed an improvement which was not greater in degree than that of the improvement which occurred in the untrained spots of the other fingers. This was the spot on the basal phalanx—"spot 3." The two remaining spots—those on the distal and middle phalanges—"1" and "2"—showed a very great improvement in the accuracy with which tactile stimuli which were applied to them were localized. If the increase in the proportion of correct answers after the training is expressed as a percentage of the correct answers which were given before the training, we obtained a measure of the degrees to which the different spots improved. The improvement of localization on spot "1" is thus about 62.5 per cent.; that on spot "2" is about 110 per cent.; and that on spot "3" is about 13 per cent.

Thus the three trained spots show very considerable variations in the improvement of localization which they exhibit. We can only say that in the case of two of them that improvement is great, and in the case of the third slight; for although the improvement of spot "1" seems from these percentages to be smaller than that of spot "2," there was no scope for greater improvement; after the training the localizations on spot "1" showed no inaccuracy at all.

The inference from this is that the three trained spots show marked independence amongst themselves, and the improvement of one of them is not accompanied *pari passu* by improvement in the others.

In this experiment the tactile stimuli were applied to similar sets of three spots on the palmar aspect of each finger. Thus the four spots "1" on the four fingers have some resemblance amongst themselves; as have also the four spots "2" and the four spots "3." A slight (apparent) general improvement in the accuracy of the localization of

tactile stimuli upon these spots occurred in the other fingers after the training of the palmar set of spots on the right index finger—was this (apparent) improvement conditioned by that training? Later in this section of the paper we analyse this apparent improvement in the untrained spots. It seems that it was possibly not a true one, but due probably to the disappearance of that type of error in which the subject indicated that he was unable to make a certain localization. Ignoring this correction, we shall here assume that the improvement was a true one.

Had it been conditioned by the training of the spots on the index finger it would have been expected that on the other fingers the improvement occurred chiefly for spots "1" and "2"—those which showed most improvement on the index finger after the training. This was not the case. Of the three spots "1" on the three untrained fingers one (on the fourth digit) showed an improvement of about 14 per cent. only; the two others were actually worse after the training of the index finger. Of the three spots "2" on the untrained fingers, one (on the fifth digit) showed an improvement of about 9·7 per cent. only; the other two were about 12 per cent. and 16 per cent. worse than before. The general improvement in the three untrained fingers was referable to an improvement in the accuracy of the localization of tactile stimuli upon the spots "3"—those which corresponded to the trained spot which showed only a slight improvement.

From this we may infer that the marked improvement in the accuracy of the localization of tactile stimuli upon two of the trained spots was not accompanied by a corresponding improvement of similar spots on the untrained fingers.

This method of analysing the errors of localization and directing the examination, as we here are doing, chiefly to possible interdependencies of errors (or of relative changes in error) is really an investigation of the possible elements in the normal process. If the changes in the accuracy of localization of tactile stimuli upon two different spots show no dependence the one upon the other these two spots to a certain extent must be regarded as functionally independent. It is true that stimuli which are applied to them may have common elements or attributes (such as the common element "right index finger" in the complete localization of two tactile stimuli applied to two different spots upon that finger); but certain of their elements must be peculiar to themselves.

Now, after the training of the spots on the right index finger, our

subject was able to localize stimuli applied to them more accurately than before. It is possible that the effect of the training was to give him a new schema of the cutaneous field upon which these spots lay; or perhaps to give him a schema in which there were only three spots, one far from the palm of the hand, one nearer the palm, and one yet more near. It is clear that such a schema would possibly serve equally well for the placing of tactile stimuli which were applied to another set of three spots on the same finger—a set obtained, as it were, by shifting our three original spots each one half-phalanx length nearer to the palm of the hand. In other words, do nearly similarly located spots on the trained finger take part in the improvement of the accuracy of localization of tactile stimuli which are applied to them?

Our results show that this is not the case. When the accuracy of localization of tactile stimuli is investigated for untrained sets of spots (which are similarly arranged to the trained spots on the finger) no improvement *pari passu* with the improvement in the trained spots occurs in them. Had such an improvement occurred it would have been expected that the “untrained” set of spots on the trained finger would have showed greater accuracy in the localization of tactile stimuli upon them than spots similarly situated on the other fingers; and that, of the three “untrained” spots on the trained finger, that which corresponded to the trained spot “1” would have shown the greatest accuracy of the three. As a matter of fact, we found that the “untrained” spots on the trained finger were far less accurately localized than the corresponding spots on the other fingers, and that, of the three untrained spots on the trained finger, the spot which corresponded to the trained spot “1” was the least accurately localized.

From this we may infer that the improvement in the localization of a set of spots on a finger after training does not extend to an untrained set of spots similarly situated relatively to one another upon the same finger.

In this first part of the experiment we also used a third set of spots on each finger—that set which lay on the dorsal aspect. The three spots of this set corresponded in position exactly (or very nearly exactly) with the ordinary spots on the palmar aspect. The only difference between the two sets was that one was situated upon the palmar and one upon the dorsal aspect of the finger.

Now the investigation of the accuracy of localization in the dorsal sets of spots on the fingers after training of one of the palmar sets of spots presents points of interest. In the first place, the training

of a set of spots on one aspect of a finger is accompanied by an increase of the accuracy with which tactile stimuli are localized upon them. Does this increase apply also to similar spots on the dorsal aspect of the same finger? In the second place, if one effect of the training of the palmar spots on the right index finger is the perfecting of the subject's schema of that part of his cutaneous field, and if at the same time the relation between that part of the field (i.e., palmar surface of right index finger) and neighbouring parts (i.e., palmar surfaces of the other fingers of the same hand) is also improved in the subject, an interesting possibility arises. The subject had before his eyes the palmar aspect of the model's right hand. To this object he related the tactile stimuli which he experienced. The right index finger was improved by education, and that lay to the right of the other three fingers. But when the spots on the back of the hand were tested, the subject looked at the dorsal aspect of the model's right hand, and then the little finger lay to the right of the other three fingers. In other words, when the relative positions in space of the four fingers are alone considered, the little finger occupies the relative position on the dorsal aspect of the pronated hand that the index finger occupies on the palmar aspect of the supinated.

After training the palmar set of spots on the right index finger the accuracy of localization of tactile stimuli on the dorsal sets of spots apparently improved for all the fingers. The (apparent) improvement was greatest for the little finger, about equally great for the index finger and ring finger, and least great for the middle finger; but in no case was the improvement comparable to that which occurred in the case of the trained palmar set of spots itself. In that trained set the chief improvement occurred in the localizing of tactile stimuli upon spots "1" and "2." In the case of the dorsal aspect of the little finger the accuracy of localization of tactile stimuli upon spot "1" was worse than before, but that of spot "2" was better. In the case of the dorsal aspect of the right index finger, improvement occurred for both spots "1" and "2," while the accuracy of localization became worse for spot "3." The improvement of spot "1" here is striking, not for its extent but because no such improvement of this spot occurred on the other fingers (save a small and negligible one on the fourth digit). Of the spots "1" on the palmar aspects of the fingers a great improvement occurred on the trained finger, a comparatively small improvement on the fourth digit again, and the localization of stimuli became worse for this spot on the second and fifth digit.

This would almost indicate that there was in fact an improvement

of localization of tactile stimuli applied to the spots on the dorsal aspect of the trained finger—an improvement conditioned by the training of the palmar set of spots. But there was a very significant difference between the two improvements. In the case of the trained set of spots, the improvement in the accuracy of localizing tactile stimuli applied to one of them was accompanied by a decrease in the number of times stimuli which were applied to the others were thought to be located upon that first spot. In other words, where a larger proportion of the stimuli applied to spot "1" were localized by the subject upon spot "1," a smaller proportion of the stimuli applied to spots "2" and "3" were localized by the subject upon spot "1." When the sets of spots on the untrained fingers were examined after training the right index finger, this did not obtain. For we then found that (with few exceptions) where improvement in the accuracy of localization of tactile stimuli occurred for a certain spot on a certain (untrained) finger, there occurred also an increase in the number of times stimuli applied to the remaining two spots on that finger were wrongly localized upon that certain spot. This relationship of the increase of accuracy in localizing stimuli applied to a spot and the increase in the error of localizing upon it stimuli applied to the other two spots was well marked in the case of the dorsal sets of spots on the right index and little fingers. In other words, whereas in the trained palmar set of spots on the right index finger increase in the accuracy of localizing tactile stimuli applied to spot "1" was accompanied by decrease in the error of localizing upon it stimuli applied to spots "2" and "3": in the untrained dorsal set of spots on that finger increase in the accuracy of localizing tactile stimuli upon spot "1" was accompanied by increase in the error of localizing upon spot "1" stimuli applied to spots "2" and "3."

We are, therefore, most probably justified in assuming that, whereas the great improvement in the localizing tactile stimuli upon the trained spots themselves is referable to the training, the smaller (apparent) improvement for the corresponding untrained spots on the dorsal aspect of the trained finger is not referable to that training, but is conditioned by some more general process. To the consideration of that general improvement we shall return later.

Thus far we have considered various facts which seem to point to the relative independence of the factors which condition the accurate localization of tactile stimuli applied to different spots on the skin, and before passing on we may notice some other phenomena which seem to point to the same conclusion.

There are two kinds of error in localization which may possibly be related to different elements in the process. Of these the first is the tendency to localize upon different spots stimuli which actually are applied consecutively to the same spot on the finger; and the second is the tendency to localize upon one and the same spot stimuli which actually are applied to different spots. The first type of error may be associated with defect in the element of "individuality" in the localization; and the second type may be associated with defect in the element of "character." In investigating these errors various relationships may be examined. For in the first place there may be a relation between the degrees of the two errors in any one finger at any one examination—that is, both errors might constantly be great or both might be small; or the relations between the two might be a reciprocal one, one being small when the other is great—or there may be no constant relation. And, in the second place, if improvement in one or both of these errors is one of the conditions of the improvement of the localization of tactile stimuli applied to the trained set of spots, another relationship may be investigated when the incidences of these errors are examined in the cases of the spots on the untrained fingers—that is, it is possible that a constant relation exists between fall in these types of error in the trained spots and fall in the untrained ones, or that no such relation exists.

There appears to be no constant relationship between the incidences of these two types of error in any one set of spots at any one examination. Sometimes the proportions of the two types of error may both be high; at other times they may both be low; at yet other times one may be low and the other high.

As the one type of error denotes defect in the element of "character" and the other denotes defect in the element of "individuality," this seems to indicate, as far as these present results go, that impairment of the element of "character" in the localization of tactile stimuli which are applied to different spots is not necessarily related, either directly or inversely, with impairment of the element of "individuality."

When we examine the incidences of the different types of error after the training of the palmar set of spots on the right index finger, we found that in the first place there was a marked fall in the error wherein the subject localized two consecutive similarly located stimuli upon two different spots. There was also a fall in the number of series of consecutive similar localizations which the subject made to dissimilarly located stimuli—although the fall was slight if analysed only in

terms of two consecutive similar localizations of stimuli applied to two different spots where the first localization was a correct one. It is probable that the improvement of localization of stimuli applied to the trained set of spots was due to reduction of both these types of error. The first of these two types of error may be termed here "individuality-error," and the second "character-error."

The decline in the incidence of individuality-error for the palmar set of spots on the right index finger was accompanied by an even greater decline for the dorsal (untrained) set of spots on the same finger. This would seem to indicate a relationship between the two sets of spots—so that the training of one of them conditioned an improvement in the localization of tactile stimuli which were applied to the other set. But in the case of the palmar and dorsal sets of spots on the right little finger a great decrease in the incidence of this type of error occurred for one set and an equally great increase in the incidence of this error occurred for the other set. This would hardly be the case if such a relationship between the two sets of spots on a finger existed, and we are perhaps correct in supposing that the training of the palmar set of spots on the right index finger was not the condition of the improvement in this type of error in the case of the dorsal set of spots on the same finger—but no positive conclusion can be drawn.

The individuality-error shows its greatest decline in incidence in the cases of the three sets of spots, the localization of stimuli applied to which showed the greatest improvement (trained palmar spots of right index finger, untrained dorsal sets of spots of index and little fingers), but there is no constant relation between the degree of improvement of localization and degree of fall of this error. The degrees of improvement of localization in the records after training the right index finger were very similar in four of the sets of untrained spots (these degrees may be denoted by the figures 2·3, 3·7, 2·4, and 2·0), but the corresponding degrees of change of the individuality-error showed marked variation (these degrees may be denoted by the figures -1·2, -8·0, +29·8, and +7·9).

After the training of the palmar set of spots on the right index finger there is therefore no constant relationship between the changes in the incidence of the individuality-error; and it may perhaps be inferred that, if the fall in the incidence of that error in the trained set of spots was conditioned by the training, that training conditioned no corresponding fall in the case of the untrained sets of spots.

Our figures for the character-error are not so definite, but in this

case also—as far as the figures go—no constant relationship between improvement in the trained spots and change in the incidence of error in the untrained ones can be drawn.

Another curious absence of relationship occurred in these experiments. After the training of the palmar set of spots on the right index finger the subject greatly improved in his localizations of tactile stimuli which were applied to them when he knew that the stimuli were being applied to these spots and to them alone. It might have been supposed that along with this improvement there would have been an improvement in the accuracy of his localization of stimuli applied to them when the stimuli were not restricted to that finger. That is to say, that when the stimuli were applied to other spots as well as to the trained ones, it would have been expected that at any rate the subject would point to the right index finger each time it was touched. We actually found that in such unrestricted tests, after the training the subject indicated the right index finger less often correctly than before the training. The test of course was not completely unrestricted, it was restricted to twelve spots—three on the palmar aspect of each finger of the right hand. We term it “unrestricted” (meaning “comparatively unrestricted”) because it was not restricted to the spots on a single finger.

The inference from this is, that in the improvement of the localization of tactile stimuli applied to the trained set of spots on the right index finger, improvement of the element of “finger” in the “position” was not one of the factors.

So far, therefore, it would seem that the improvement in the localization of tactile stimuli applied to the trained spots is not only restricted to that set of spots, but that it is a special and independent process for each of the trained spots. We must now refer to the results of one test which seem to contradict this.

When the subject localized stimuli applied to the ordinary spots on the palmar surfaces of the four right fingers without knowing to which spot or to which finger the stimulus was applied, it was found that the accuracy of localizing the spots (without taking account of the accuracy of localizing the finger on which they lay) was much greater than it was expected it would be. We had thought it possible that the proportion of correct replies to this part of the questions put to the subject would approximate to the average of the proportions for the spots on the four fingers when these were tested separately in the ordinary test—where the subject knew to which finger the stimuli were being applied. We thus expected that, where the localization for the

spots of one finger was very inaccurate, and where it was comparatively accurate for the spots of another finger, as these spots were equally often touched in the unrestricted finger test the accuracy of localization there would be the mean of the accuracies for the separate fingers in restricted finger test. Indeed it might have been expected to be less if hazard came into the localization; for the hazard error in the test of a single finger is 66.7 per cent., whereas in the unrestricted finger test it is 91.7 per cent. As a matter of fact, we found that this error was much less than the average of the errors for all the fingers in the restricted test, and that actually it approximated, both before and after training, most closely to the error of the most accurately localized set of spots in the restricted test.

This result (which in this case was most striking, but which we have not obtained in another similar case) was quite an unexpected one. After the training of the palmar set of spots on the right index finger that was the most accurately localized set, and the average error of localization fell most markedly for it. In the unrestricted test there was a corresponding increase in the accuracy of localization of the spots touched as regards the place on the finger (that is, as regards the position of the spot in the set) and irrespective of the accuracy of localizing the finger.

The inference from this would seem to be that as regards this specific case, the training of one set of spots was accompanied by an improvement of the element "place on finger" in the localization of tactile stimuli which were applied to them and that this improvement extended to other and untrained spots, but only (or only markedly) when the test was not restricted to a single finger.

It is not difficult to see how such a general improvement may have occurred. The three spots on each finger occupied similar positions relatively to the parts of the finger—one spot lay in the middle of each obvious part or segment of the finger. The training of the spots of one set no doubt improved the subject's schema of their positions; it improved, as it were, the element "place on finger" in the "positions" of the touches. But that element is common to the spots of the untrained sets, and its improvement for one set may well have conditioned improvement for other and untrained sets of spots. The difficulty is to see how, in this case and at this period in the experiment, the improvement occurred only when the test was one unrestricted as regards the fingers to which the tactile stimuli were applied—but restricted to the three spots on each finger.

The occurrence of "positive error" in the localization of the finger (apart from the localization of the place of the spot on the finger) in this test gives us a hint as to the reason for this curious restriction of the improvement. In the unrestricted test it was found that the subject more often localized the tactile stimuli upon certain fingers than upon others, and that the error in localizing finger alone was in some cases considerably greater than the error of hazard. In other words the subject had a definite bias against the localization of stimuli upon certain fingers. The restriction of the test to a single finger (when that was done) no doubt brought in a complicating factor; for the subject knew that the tactile stimuli were applied to a certain finger, and might yet feel that the touches were on another finger. In making his decision, for instance, of the localization of a touch applied to spot "2" on a certain finger, he might think that the touch (which felt, for example, as if it was on spot "2" of another finger) most resembled one applied to spot "3" on the finger to which he knew that the stimuli were being applied. Thus he might make an incorrect localization of the place of the touch upon the finger, although—had the test been unrestricted as regards the fingers—he would have placed the touch in the correct position upon the finger, but on the wrong finger. It is therefore possible that in the unrestricted finger test a complication was removed, and this common element of "place on finger" in the "position" of the touches was so freed that the improvement in it conditioned by the training of one set of spots was extended to others.

We may now consider the nature of the improvement of localization of tactile stimuli which followed the training of the spots on the palmar aspect of the right index finger. That improvement occurred not only in the case of the trained set of spots, but also in the case of some of the sets of spots on the untrained fingers.

In the case of the trained set of spots the records show a decrease both in the character-error and in the individuality-error after the training. Thus, after that training, when tactile stimuli were applied to the three spots in such an order that no two consecutive stimuli were applied to the same spot, on the whole there were fewer consecutive similar answers given—on fewer occasions after the training were consecutive dissimilar stimuli localized by the subject upon the same spot on the model. At the same time, when tactile stimuli were applied to the three spots in such a manner that two or more consecutive stimuli were given to the same spot, there were, upon the whole, fewer consecutive dissimilar answers.

But in our results there was also a reduction in one of the position-errors. The abolition of the character-error—so that the subject was always able to say correctly whether or not a certain tactile stimulus was applied to that same spot on the skin to which an immediately preceding stimulus had just been applied—if unaccompanied by improvement in the other factors in localization would easily be recognized in the records. For where series of tactile stimuli were given so that no consecutive two were applied to the same spot, the answers would also show series in which no consecutive two answers were similar, but tactile stimuli applied at different times to any one spot would be localized now upon one spot of the three, and now upon another. The error in the localization of tactile stimuli applied to a certain spot of the three would be the error of hazard—66.7 per cent., and of the answers to these stimuli 33.3 per cent. would be localizations on each of the two possible wrong positions. If, however, there was also abolition of the individuality-error the errors of localization would be expected to become constant. Stimuli applied to spot “3” might thus always be localized upon spot “2,” and so on. In such a case the error of localization of stimuli applied to a certain spot in a series of records would be the error of hazard if the individuality of the tactile stimuli applied to that spot varied from day to day. In any case the answer to stimuli applied to a spot would be expected to be constant for any one record, and the average error for all the spots tested would be expected to be the error of hazard.

Our records give no approximation in error to the error of hazard after the training of the spots. The inference is that along with the reduction of the character-error and the individuality-error there is a reduction of the position-error. As reduction of the character-error occurred to an even greater extent in the case of certain of the untrained sets of spots; and as reduction of the individuality-error occurred to an even greater extent in the case of certain other sets of untrained spots; but, as, nevertheless, the reduction of the total error of localization of the untrained sets of spots was in no case comparable with the reduction of this error in the case of the trained set of spots, we are inclined to think that the improvement in the localization of tactile stimuli applied to the trained spots was chiefly due to improvement in the element of “position.”

Improvement in the localization of stimuli which are applied to a certain spot would be expected to have a reverse as well as an obverse side. In the first place, stimuli applied to that spot are less often

localized by the subject upon other spots: and in the second place, stimuli applied to other spots would be expected to be less often localized by the subject upon the spot. If the character and the individuality of stimuli applied to the spots are alike improved, and if at the same time there is an improvement in the position—in the correct placing upon the finger—of each of these stimuli, the stimuli applied to a certain spot will less often be localized upon another, and the stimuli applied to the other spots less often upon the first.

Of the three trained spots, spot "1" showed a very definite improvement in the localization of tactile stimuli which were applied to it. They were always correctly localized after the training—so that the error of localizing upon the other two spots touches which were applied to spot "1" fell to zero. At the same time there was a reduction of the errors of localizing stimuli applied to either of the other two spots upon this spot. After the training spot "2" showed also a great improvement in the localization of tactile stimuli applied to it. The error of localizing touches of this spot upon either of the other two spots ("1" and "3") fell considerably; but, while there was a reduction of the error of localizing touches of spot "1" upon this spot (a reduction to zero), there was actually a small increase of the error of localizing touches of spot "3" upon it. Spot "3" itself showed a comparatively small improvement in the localization of tactile stimuli applied to it. The error of localizing touches of this spot upon spot "1" fell slightly (the reduction being much less than that of the error of localizing touches of spot "2" upon spot "1"), but the error of localizing touches of spot "3" upon spot "2" actually rose slightly. The errors of localizing touches of spot "1" and "2" upon this spot "3" showed, as we have said above, great reductions.

From these differences in the improvement of the accuracy of localization of tactile stimuli upon spots "1" and "2," on the one hand, and spot "3" upon the other, it may perhaps be inferred that the training comparatively failed in the case of the last, and that the slight improvement was due to some other process than that which occurred in the two former. Again it must seem as if the obverse and the reverse of the improvement in the localization of tactile stimuli which are applied to a trained spot are not interdependent. Thus a great improvement in the localization of tactile stimuli which are applied to a certain spot (spot "2") is accompanied by a decrease in the error of localizing these stimuli upon a certain other spot (spot "3"), but there is no corresponding decrease (and indeed there is actually an increase) in the error of

localizing tactile stimuli which are applied to that certain other spot ("3") upon the first spot ("2"). The subject as it were recognizes more clearly touches which are applied to a certain spot, but this more clear recognition does not necessarily help him to realize that touches which are applied to another spot are not applied to the first spot. In other words the improvement of localization of tactile stimuli which are applied to a certain spot is not necessarily accompanied by a corresponding improvement for other spots on the same aspect of the same finger. It would appear as if each spot is improved for itself without reference to the others. Where the improvement occurs in two spots there is a mutual relationship—"obverse" and "reverse"—in the reduction of the errors of localization of the two; but where only one of a pair of spots shows a great improvement no such mutual relationship may occur.

In addition to the special improvement in the localization of tactile stimuli which occurred in the case of the trained spots, there occurred a less marked general (apparent) improvement in localization for the untrained sets of spots on the other fingers—and on the dorsal aspects of all the fingers. In what did this consist?

A most marked change which synchronized with the period of training was the disappearance of error due to "confusion." Before the training the subject repeatedly indicated that he was unable to come to a decision with regard to the localization of certain stimuli. After the training, on scarce an occasion did he fail to make a localization of some sort, and the disappearance of this source of error was a general one—it extended to stimuli applied to the untrained as well as to the trained sets of spots. It is clear that even if the subject had hazarded his localizations of the touches of which he was not certain, this would have led to a reduction of the percentage error of localization—for a certain proportion of these touches would then have been bound to be correct. If, however, we speculate that the "confused" touches were (after the disappearance of the "confusion" error from the records) really localized in the same proportion (as between "right" and "wrong") as the definitely localized touches before the disappearance of the "confusion" error; and, having found the proportion of the "confused" answers which corresponds with the proportion of wrong definite localizations before the disappearance of "confusion," we then add the two together, it is found that the resultant corresponds very definitely with the proportion of definite wrong localizations made in the records after the disappearance of the "confusion" error as far as the untrained sets of spots are concerned. This is demonstrated in Table

XXXIII. It is there seen that except in the case of the trained set of spots on the palmar aspect of the right index finger the percentage error of localization for the untrained sets of spots (after the disappearance of the "confusion" error) is very nearly what it would have been had the same proportion of the previously "confused" touches, as of the previously definitely localized touches, been wrongly localized. In the localization of touches on the palmar sets of spots the actual error is slightly greater than it would have been if this had been exactly the case; a yet closer approximation occurs in the case of the dorsal sets of spots, but only in the case of the dorsal set of spots on the little finger ("R 5") is the actual error less than the computed.

It will be remembered that there was some evidence to show that in the case of one of the trained spots the improvement of localization was probably not very largely conditioned by the training—spot "3." In Table XXXIII the figures for the three individual spots of the trained set are also given. It is seen that in the case of spots "1" and "2" the actual error of localization after the training (and after the disappearance of the "confusion" error) is very much less than it would have been if the decline in error had been due solely to the correct localization of a proportion of the touches which before had been "confused." But in the case of spot "3" we again obtain a close approximation between the actual error and the error computed as above (that is, by adding to the proportion of definitely wrongly localized touches before the training the corresponding proportion of the un-localized or "confused" touches). Here, however, the actual error is slightly less than the computed.

This all seems to point to the fact that the apparent improvement in the localization of tactile stimuli upon the untrained spots (and upon one of the trained ones) is really due to the disappearance of the "confusion" error—that it is not a real general improvement. The figures throw into an extremely strong light the great change which took place in the case of two of the trained spots—a change which we think can be ascribed to the training. We think that the apparent improvement in the cases of the untrained sets of spots is, at this stage in the experiment, not a real one; but we say this with the knowledge that later a real improvement occurred.

This seems to dispose of the question of the apparent general improvement in localization of touches applied to the untrained sets of spots, but certain changes took place in the incidence of error amongst them after the training of the right index finger—and these changes are of interest. In some cases the proportions of correct localizations for

the touches applied to the individual spots on the untrained fingers showed differences in the records before and after the training of the palmar set of spots on the right index finger. But, whereas in the case of the trained spots the increase in the proportion of correct answers for a spot was, on the whole, accompanied by decrease in the wrong localizations upon it of touches applied to other spots, in the case of the untrained spots a rise in the proportion of correct localizations for a certain spot was almost always accompanied by a rise in the proportion of times touches applied to other spots were localized upon it. This really means that, after the training, the subject was more apt to place any tactile stimulus upon a certain spot than before it. Thus in the cases of the dorsal sets of spots there was a greater tendency to give the answer spot "2" (whether it was right or wrong) after the training than before it. The increase in the proportion of times spot "2" was given as an answer (which was accompanied by an increase in the proportion of correct localizations of touches applied to that spot) was accompanied by a decrease in the proportion of answers spot "1," and by a decrease in the proportion of answers spot "3." It occurred, as it were, at the expense of the answers spot "1" and spot "3," and at the expense of the answer "confused." Here we have a definite tendency to a certain localization—which would not be expected to be the case had the answers merely been selected by hazard.

In connection with this definite change in the numerical proportion of the different answers to the touches it must, however, be noticed that both before and after the training of the right index finger there was a greater tendency to make the wrong localizations of touches of spot "1" upon spot "2" than upon spot "3"; and a corresponding greater tendency to make the wrong localizations of touches of spot "3" upon spot "2" than upon spot "1." That is to say, that when one of the terminal spots of the set of three was wrongly localized it was more often referred to the middle spot—that nearest to it—than to the spot at the other end of the set. Had a general improvement occurred in the localization of touches upon the untrained spots it might have been expected that, along with a greater proportion of correct answers to touches upon each of the terminal spots of the sets, there would have been a reduction of the incorrect references to the spot at the other end of the set and an increase in the incorrect references to the middle spot—as it were, a partial improvement in the accuracy of localization. Had this occurred the number of answers spot "2" both to touches

applied to that spot itself and to touches applied to the spots at the two ends of the set (spots "1 and 3") would have increased. But as a matter of fact the increase in the number of answers spot "2" in the case of the untrained dorsal sets of spots increased along with a decrease in the correct localizations of touches applied either to spot "1" or spot "3" or both to the touches applied to these two spots. We are, therefore, justified in the assumption that the increase in the number of answers spot "2" in the case of tactile stimuli applied to these untrained sets of spots was not due to a partial general improvement of localization, but to a definite tendency to refer the touches rather to that spot than to the others—an approximation to "positive error."

On the whole, then, we may say that proper analysis seems to eliminate the occurrence of a general improvement of the localization of tactile stimuli which were applied to the untrained sets of spots (and perhaps also to one of the trained spots): and that it seems to show that the improvement in the case of two of the trained spots was due either to the effect of the training or to some other change which did not affect the untrained sets of spots.

It is thus possible that the conditions of the experiment more favoured the accuracy of localization of touches upon the set of spots which we selected for training than that of the touches upon the untrained sets of spots; and it is also possible that the conditions of the cortical (or cerebral) lesion were not stable, and that by chance the change effected an increase of the accuracy of localization for the trained spots only.

Thus, in the first place, we investigated the fingers in a constant order. First, the palmar surfaces of two of the normal fingers were tested; then, in order, the palmar surfaces of the four affected fingers—beginning with the right index finger; then the dorsal surfaces of two of the normal fingers; and finally the dorsal surfaces of the four affected fingers—again commencing with the right index finger.

It is thus possible that a process of "general fatigue" may have so complicated the results that the fingers first tested may have appeared more accurate in localization than those last tested. But our records give little indication that this was the case. In the first place the records before the training of the right index finger should then have shown the same progressive changes as those taken after it. This is not the case. The first affected finger to be tested shows then greater inaccuracy than the second: the third than the fourth. In the second place the different fingers might have been expected to show a definite

descending order of improvement of localization in the order in which they were tested. This, again, is not the case. Thirdly, in this part of the experiment we constantly used as a control one of the normal fingers, testing the accuracy of localization of tactile stimuli upon it at the end of the record, when general fatigue would be expected to be at its maximum. The accuracy was seldom found to be less than at the commencement of the test. Fourthly, on one occasion we repeated the test of the right index finger at the end of the record, and the accuracy of localization was then found to be greater than before. On the whole, we may say that, although there probably was some process of general fatigue, it cannot be regarded as the explanation of our results.

But we cannot, on the evidence furnished by this part of the experiment alone, eliminate the possibility that the improvement of the localization of tactile stimuli applied to the trained spots may have been due to some change in the condition of the central lesion—a change associated only by chance with the training of the spots. We think, however, that this possibility must be eliminated in view of the data we obtained in subsequent parts of the experiment. For, later on in it we selected another finger—the fourth right digit—and found that improvement in the localization of tactile stimuli applied to its palmar set of spots also occurred during and after training. As the error of localization of tactile stimuli upon the spots of this finger was large before that training—as it was, indeed, larger than that of any other set of spots in this first part of the experiment—and, as after the training, it became only less small than the error in the case of the finger which we first trained, we think that this disposes of the possibility that the results which we have described here were due to a change not connected with the training. We do not claim, however, that no such change, or that no general improvement in the localization of tactile stimuli occurred throughout the whole course of the experiment.

V.—ANALYSIS OF THE FIRST SERIES OF TESTS, DURING WHICH AN ATTEMPT TO EDUCATE SPOTS IN ACCURACY OF LOCALIZATION OF TACTILE STIMULI WAS MADE.

(1) *In General.*

In this series of tests two sets of three different spots were selected for examination in each of the second, third, fourth, and fifth digits of the affected right hand, and on the third and fourth digits of the

"normal" left hand. Of these two sets, in each case one lay on the palmar aspect and one on the dorsal; the three spots of each set lay on the skin of the finger in its dorsi-ventral axial plane, one being opposite the mid-point of each of the three phalanges. For the purposes of a small number of tests, a third set of three spots was chosen on the palmar aspects of each of the four fingers of the right hand. These also lay on the skin in the dorsi-ventral axial plane of the finger, but they were placed on the folds of skin at which the finger bends, and which lie near to the metacarpal-phalangeal and the two interphalangeal joints.

In the records care had not been taken to assure that each spot on a finger in the test was stimulated the same number of times, and the number of times a specific spot was stimulated in different records varied. As the experiment proceeded, we found that the accuracy of localization of tactile stimuli was not the same for the three different spots on a finger—it was, for instance, sometimes most defective for spot "3" (that nearest the trunk) and least defective for spot "1" (that nearest the tip of the finger). It is thus clear that a record in which spot "1" is stimulated more often than spots "2" or "3" may give a different percentage of error than one in which spot "3" is most often stimulated. In estimating the error of localization in a record in this series of observations, we have, therefore, used the "average percentage error" which is obtained by finding the "percentage error" for each of the three individual spots, and taking the average of the three percentages. As there was not, however, a large preponderance of the times any one individual spot was stimulated in any one record, this does not markedly differ from the percentage error of the record; the difference between the percentage error and the "average percentage error" in the records is usually less than 1 per cent., and rarely greater than 2 per cent.

(2) *On the Records which were taken before Training commenced.*

For the first to the fifth day of the series the tests were applied in the ordinary manner to the spots on the palmar and dorsal aspects of the fingers. The following table, in which L 3 and L 4 stand for the digits of the left hand, and R 2, R 3, &c., for those of the affected right hand, gives the "average percentage error" of localization for the spots on the palmar and dorsal aspects of the different fingers on the five different days—twenty-five stimuli applied in an indiscriminate order being given to the three spots on each aspect of each of the fingers which were tested:—

TABLE I.—“AVERAGE ERROR PER CENT.” FOR LOCALIZATION OF TACTILE STIMULI ON THE PALMAR AND DORSAL SETS OF SPOTS OF EACH FINGER ON EACH OF THE FIVE DAYS WHICH IMMEDIATELY PRECEDED THE ATTEMPT TO TRAIN THE PALMAR SPOTS ON THE RIGHT INDEX FINGER. EACH FIGURE IS CALCULATED FROM TWENTY-FIVE ANSWERS—EXCEPT THE AVERAGES AND MEAN VARIATIONS IN THE RIGHT-HAND COLUMNS.

Finger	DAY OF EXPERIMENT					Average	Mean variation
	1	2	3	4	5		
Palmar L 3 ..	7.4	0.0	0.0	0.0	0.0	1.48	2.37
L 4 ..	0.0	0.0	14.3	0.0	8.3	4.52	5.42
R 2 ..	35.4	41.8	50.9	44.0	41.4	42.70	3.80
R 3 ..	31.7	17.6	38.7	25.9	46.0	31.98	8.30
R 4 ..	39.0	40.0	46.3	47.3	61.1	46.72	5.96
R 5 ..	46.0	44.0	33.3	36.9	55.1	43.06	6.37
Dorsal L 3 ..	0.0	0.0	0.0	0.0	3.3	0.66	1.06
L 4 ..	4.3	3.3	0.0	2.6	0.0	2.04	1.63
R 2 ..	25.4	30.7	20.4	44.4	21.9	28.56	7.19
R 3 ..	19.0	11.4	20.9	21.7	20.8	18.76	2.94
R 4 ..	43.5	15.0	17.6	26.9	31.0	26.80	8.40
R 5 ..	27.0	27.8	20.0	53.1	35.2	32.62	9.22

It will be observed that for their palmar aspects the arrangement of the right digits in order of decreasing accuracy of localization of tactile stimuli is: R 3, R 2, R 5, R 4; the corresponding order for the dorsal aspects is: R 3, R 4, R 2, R 5; and the most accurate finger for either aspect is R 3.

The second table gives the average percentage error for each individual spot on each finger in this same series of records:—

TABLE II.—THE TOTAL PERCENTAGE ERROR OF LOCALIZATION FOR EACH OF SPOTS “1,” “2,” AND “3” ON THE PALMAR AND DORSAL ASPECTS OF EACH OF THE FINGERS EXAMINED ON THE FIVE DAYS WHICH IMMEDIATELY PRECEDED THE TRAINING. EACH PERCENTAGE IS CALCULATED FROM ABOUT FORTY-TWO OBSERVATIONS.

Finger	NUMBER OF INDIVIDUAL SPOT.		
	1	2	3
Palmar L 3 ..	0.00	2.17	2.63
L 4 ..	0.00	0.00	15.38
R 2 ..	32.43	62.50	35.00
R 3 ..	13.33	26.32	59.52
R 4 ..	25.71	31.37	79.49
R 5 ..	37.78	46.67	40.00
Dorsal L 3 ..	2.38	0.00	0.00
L 4 ..	4.65	1.82	0.00
R 2 ..	45.95	25.00	15.00
R 3 ..	15.56	34.21	9.52
R 4 ..	31.43	33.33	20.51
R 5 ..	37.78	40.00	17.14

It will be observed that in the case of fingers R 3, R 4, the accuracy of the localization of tactile stimuli on spot “3” (that nearest the

trunk) on the palmar aspect is markedly less than that on spots "1" and "2"; while the accuracy of the localization on spot "1" is markedly greater than that on spot "2." In the case of the other two fingers (palmar aspects) the accuracy of localization of tactile stimuli is worst for spot "2," and about equal on spots "1" and "3." When the figures for the dorsal aspects of the right digits are examined, it is seen that in every case the accuracy of localization is least defective on spot "3" (that nearest the trunk), and, except in the case of R 2, most defective on spot "2."

The average percentage error for the localization of tactile stimuli on spot "3" of the palmar aspect of the fourth right digit—R 4—is a figure of interest. That percentage is 79·49—markedly greater than the error of hazard, which is here 66·67 per cent. The following table expands this figure:—

TABLE III.—PERCENTAGE ERROR OF LOCALIZATION FOR SPOT "3" ON THE PALMAR ASPECT OF THE FOURTH RIGHT DIGIT, "A" IN EACH OF THE FIVE RECORDS BEFORE, AND "B" IN EACH OF THE FIVE RECORDS AFTER, "TRAINING" THE SECOND RIGHT DIGIT.

Record		A			Record		B
1	..	62·50	9	..	100·00
2	..	75·00	10	..	50·00
3	..	100·00	11	..	54·55
4	..	90·91	12	..	66·67
5	..	75·00	13	..	77·78

It will be seen that on only one occasion—the first—was the average error for this spot less than that of hazard. This is an instance of "positive" error in localization. It is markedly greater than the error which would occur if the subject had no idea which of the three spots was touched, and indicated any one of them indiscriminately by chance.

The kind of answer which was given in these cases to a tactile stimulus which was applied to spot "3" is of interest. Each time the spot was touched the subject gave one of four possible answers with regard to its localization. In the first place the answer might be correct, and the subject then indicated correctly the corresponding spot on the hand of the model. In the second place the subject might be unable to make a localization (he then tapped the table). While in the third and fourth places the subject might make a wrong localization—indicating either spot "1" or spot "2" on the model as that corresponding to the spot touched. The following table gives the average number of times per cent. each of these answers was given:—

TABLE IV.—ANALYSIS OF THE KIND OF ANSWERS GIVEN WHEN SPOT "3" ON THE PALMAR ASPECT OF THE RIGHT FOURTH DIGIT WAS TOUCHED IN THE RECORDS DETAILED IN TABLE IV, GIVING TOTAL NUMBERS AND PERCENTAGES FOR THE TWO SETS OF RECORDS, "A" AND "B."

Answer	A (Records 1 to 5)		B (Records 9 to 13)	
	No.	Per cent.	No.	Per cent.
Right —i.e., "3"	8	20.51	14	30.43
Confused	4	10.25	0	0.00
"1" instead of "3"	1	2.56	2	4.35
"2" instead of "3"	26	66.67	30	65.22
	39	99.99	46	100.00

Had they been selected by hazard the percentage in each case would have been about 25.00; as it is, it is seen that the wrong answer "2" for "3" is given in two-thirds of the cases. The positive error in the localization of tactile stimuli applied to spot "3" on the subject is, therefore, very largely conditioned by his mistaking the locus of the stimulus for that of stimuli applied to spot "2."

The number of times "confusion" occurred in the record for the palmar and for the dorsal set of spots of each finger on each of the first five days is given in the table below. The total number of stimulations in each case was 25 for the set of palmar spots, and the same number for the dorsal:—

TABLE V.—THE NUMBER OF TIMES (OUT OF TWENTY-FIVE OBSERVATIONS IN EACH CASE) NO LOCALIZATION COULD BE MADE—"CONFUSION"—FOR EACH OF THE PALMAR AND DORSAL SETS OF SPOTS OF EACH FINGER ON EACH OF THE FIVE DAYS WHICH IMMEDIATELY PRECEDED THE TRAINING.

			DAY OF EXPERIMENT							
Finger			1	2	3	4	5			
Palmar	L 3	..	0	..	0	..	0	..	0	0
	L 4	..	0	..	0	..	0	..	0	0
	R 2	..	0	..	2	..	3	..	6	8
	R 3	..	0	..	0	..	2	..	0	5
	R 4	..	0	..	1	..	3	..	4	5
Dorsal	R 5	..	0	..	0	..	3	..	3	4
	L 3	..	0	..	0	..	0	..	0	0
	L 4	..	0	..	0	..	0	..	0	0
	R 2	..	0	..	1	..	2	..	8	3
	R 3	..	0	..	1	..	2	..	2	6
	R 4	..	0	..	2	..	1	..	3	5
	R 5	..	0	..	1	..	2	..	7	6

The apparent absence of "confusion" on the first day is due to the fact that the subject did not clearly realize that he was to tap the table when he was unable to make a localization; on this day it is probable that a certain number of his answers were guesses. We think that

this is the only occasion in the experiments on which he guessed an answer.

A remarkable feature of the early experiments was that on the one hand the subject repeatedly localized successive differently located tactile stimuli on the same spot, and that, on the other hand, he repeatedly localized successive similarly located tactile stimuli on different spots.

It is difficult to make an analysis of these types of error. It may be attempted by scrutinizing the answers to consecutive similar pairs of tactile stimuli, but this makes no account of instances in which different replies are given in series of similar stimuli; or in which the same reply is made many times in succession when different spots are touched. We have observed a marked tendency for a series of similar replies to be given to a series of different tactile stimuli; and when a series of similar stimuli has been given there is a tendency for the type of reply to persist, and for the subject thus wrongly to localize a dissimilar stimulus which is applied immediately after the series.

In the following table the number of times two different answers were given to two consecutive similar stimuli is given as a percentage of the number of times pairs of similar stimuli were given in a test—these percentages being given for the dorsal and palmar sets of spots on each finger on the first five days of the experiment:—

TABLE VI.—THE PERCENTAGE NUMBER OF TIMES PAIRS OF TWO CONSECUTIVELY SIMILARLY LOCATED STIMULI WERE LOCALIZED ON TWO DIFFERENT SPOTS; GIVEN FOR EACH ASPECT OF EACH FINGER ON EACH OF THE FIVE DAYS WHICH IMMEDIATELY PRECEDED THE TRAINING.

		DAY OF EXPERIMENT.											
Finger		1	2	3	4	5	Average S.D.		Mean variation				
Palmar	L 3	.. 40.0	.. 0.0	.. 0.0	.. 0.0	.. 0.0	= 8.0	.. 12.8					
	L 4	.. 0.0	.. 0.0	.. 25.0	.. 0.0	.. 0.0	= 5.0	.. 8.0					
	R 2	.. 50.0	.. 20.0	.. 20.0	.. 60.0	.. 50.0	= 40.0	.. 16.0					
	R 3	.. 40.0	.. 0.0	.. 50.0	.. 20.0	.. 62.5	= 34.5	.. 19.6					
	R 4	.. 33.3	.. 50.0	.. 25.0	.. 33.3	.. 20.0	= 32.3	.. 7.9					
Dorsal	R 5	.. 16.7	.. 11.1	.. 28.6	.. 25.0	.. 60.0	= 28.3	.. 12.8					
	L 3	.. 0.0	.. 0.0	.. 0.0	.. 0.0	.. 14.3	= 2.9	.. 4.6					
	L 4	.. 12.5	.. 0.0	.. 0.0	.. 25.0	.. 0.0	= 7.5	.. 9.0					
	R 2	.. 25.0	.. 60.0	.. 20.0	.. 60.0	.. 25.0	= 38.0	.. 17.6					
	R 3	.. 0.0	.. 25.0	.. 16.7	.. 40.0	.. 37.5	= 23.8	.. 12.4					
	R 4	.. 33.3	.. 0.0	.. 37.5	.. 16.7	.. 40.0	= 25.5	.. 13.7					
	R 5	.. 0.0	.. 44.4	.. 57.1	.. 100.0	.. 40.0	= 48.3	.. 24.2					

In Table VII the number of times two consecutive stimuli applied to different spots were localized by the subject upon the same spot is given for each record on each of the first five days of the experiment. In

each record of 25 successive tactile stimuli there were about twenty occasions in which two successive stimuli were applied to different spots on the subject :—

TABLE VII.—THE NUMBER OF TIMES TWO DIFFERENT CONSECUTIVE STIMULI WERE LOCALIZED UPON THE SAME SPOT—GIVEN FOR THE PALMAR AND DORSAL SETS OF SPOTS OF EACH FINGER ON EACH OF THE FIVE DAYS WHICH IMMEDIATELY PRECEDED THE TRAINING.

		DAY OF EXPERIMENT												Average	Mean variation
Finger		1		2		3		4		5					
Palmar L	3	..	0	..	0	..	0	..	0	..	0	=	0.0	..	0.0
	L 4	..	0	..	0	..	2	..	0	..	2	=	0.8	..	0.96
	R 2	..	8	..	9	..	5	..	1	..	4	=	5.4	..	2.5
	R 3	..	6	..	5	..	3	..	7	..	3	=	4.8	..	1.4
	R 4	..	6	..	10	..	2	..	4	..	6	=	5.6	..	2.1
Dorsal L	R 5	..	8	..	4	..	5	..	8	..	9	=	6.8	..	1.8
	L 3	..	0	..	0	..	0	..	0	..	0	=	0.0	..	0.0
	L 4	..	1	..	2	..	0	..	1	..	0	=	0.8	..	0.6
	R 2	..	5	..	4	..	3	..	4	..	3	=	3.8	..	0.6
	R 3	..	5	..	2	..	6	..	4	..	0	=	3.4	..	1.9
Dorsal R	R 4	..	8	..	3	..	4	..	3	..	3	=	4.2	..	1.5
	R 5	..	6	..	5	..	4	..	5	..	2	=	4.4	..	1.1

The variation of the results here is in part due to the variation in the number of times in a record the subject was unable to make a localization—as these have not been included in the table.

But, with regard to this type of error, it must be noted that it is of two distinct forms, one of which may be regarded as a more inaccurate type than the other. Thus when two consecutive tactile stimuli are applied to two specific different spots on the skin the subject may localize the first wrongly, but may “correct” his error at the second stimulus (if that happens to be applied to the spot to which the subject had localized the first stimulus). Thus similar replies may be given to two different stimuli. But the error would be one of a different type if the subject correctly localized the first stimulus and then incorrectly localized the second stimulus (applied to another spot) on the same spot as the first. But here also his replies to differently located stimuli would be similar. In other words, when the instances in which the subject replies with the same answer to two consecutive differently located stimuli are examined a distinction should be drawn between those cases in which the first of the two stimuli is correctly localized and those in which the second is. In the following table (VIII) the numbers of occasions on which the subject correctly localized the first of a pair of different stimuli and then located the second stimulus at the same spot as the first are given :—

TABLE VIII.—THE NUMBER OF TIMES THE SECOND OF A PAIR OF DISSIMILAR CONSECUTIVE STIMULI WAS WRONGLY LOCALIZED ON THE SAME SPOT AS THAT ON WHICH THE FIRST OF THE PAIR HAD BEEN CORRECTLY LOCALIZED—GIVEN FOR THE PALMAR AND DORSAL SETS OF SPOTS OF EACH FINGER ON EACH OF THE FIVE DAYS WHICH IMMEDIATELY PRECEDED THE TRAINING. THE NUMBERS ARE OUT OF ABOUT TWENTY OBSERVATIONS EACH.

Finger	DAY OF EXPERIMENT					Average	Mean variation
	1	2	3	4	5		
Palmar L 3	2	0	0	0	0	0.4	0.64
L 4	0	0	0	0	1	0.2	0.32
R 2	3	3	3	0	3	2.4	0.96
R 3	3	3	2	4	2	2.8	0.64
R 4	3	6	1	1	2	2.6	1.52
R 5	6	3	2	4	3	3.6	1.12
Dorsal L 3	0	0	0	0	0	0.0	0.00
L 4	1	1	0	1	0	0.6	0.48
R 2	2	3	1	3	1	2.0	0.80
R 3	3	1	3	2	0	1.8	1.04
R 4	3	1	3	2	1	2.0	0.80
R 5	3	4	2	3	1	2.6	0.88

(3) *On the Records which were taken during the Training.*

On three successive days the spots of the palmar set on the right index finger were trained for the localization of tactile stimuli in the manner described before. Records of the accuracy of localization of tactile stimuli on these spots were taken immediately before and immediately after the training and showed uniformly a slightly greater defect immediately after the training.

TABLE IX.—“AVERAGE ERROR PER CENT.” OF LOCALIZATION OF THE SPOTS ON THE PALMAR ASPECT OF THE RIGHT INDEX FINGER BEFORE, IMMEDIATELY AFTER, AND THEN AT HOUR INTERVALS AFTER TRAINING.

Time	“Average error per cent.”			
9.45 a.m.	37.2
10.50 „	35.2
“TRAINING.”				
11.8 a.m.	46.7
12.3 p.m.	40.6
12.57 „	38.9
2 „	30.3
3.10 „	27.6
4 „	32.5
5.3 „	20.0
6 „	19.3
6.54 „	12.2
7.45 „	15.4
8.52 „	25.0

On the third of these days we gave the training in the morning, and thereafter repeated the test of the accuracy of localization of tactile stimuli on the trained spots after each interval of one hour which elapsed. The percentage error of localization gradually decreased (having been considerably higher immediately after the training) and at its least was about one-third only of the lowest previous error on this finger. Table IX gives these average percentage errors.

But when the spots on the palmar aspects of the other fingers were tested at the end of the day, it was found that improvement of the accuracy of localization of tactile stimuli had occurred in every case. This is shown in Table X:—

TABLE X.—“AVERAGE ERROR PER CENT.” OF LOCALIZATION OF THE SPOTS ON THE PALMAR ASPECTS OF EACH OF THE FOUR RIGHT FINGERS BEFORE AND AFTER THE RECORDS GIVEN IN TABLE IX.

Palmar	Finger	Before	After
L 3	..	0·0	3·0
R 2	..	37·2	25·0
R 3	..	42·9	30·1
R 4	..	50·0	23·3
R 5	..	57·2	41·1

TABLE XI.—“AVERAGE ERROR PER CENT.” OF LOCALIZATION OF THE SPOTS ON THE PALMAR ASPECT OF THE RIGHT INDEX FINGER AT DIFFERENT INTERVALS OF TIME THROUGHOUT THE DAY.

Time		Four-hour (9)	Three-hour (10)	Half-hour (12)
10 a.m.	..	—	15·1	7·6
10.30 „	..	16·7	—	—
11 „	..	—	—	—
11.30 „	..	—	—	23·1
12 m.d.	..	—	—	27·9
<i>Dinner.</i>				
12.30 p.m.	..	—	—	26·1
				(Finished dinner)
1 „	..	—	7·2	28·1
				(Half pipe)
1.30 „	..	—	—	11·4
2 „	..	—	—	25·8
				(Pipe)
2.30 „	..	4·8	—	27·2
3 „	..	—	—	25·0
3.30 „	..	—	—	16·9
				(Pipe)
4 „	..	—	7·9	28·6
				(Sleeping)
4.30 „	..	—	—	15·9
5 „	..	—	—	36·7
<i>Tea.</i>				
5.30 „	..	—	—	13·3
6 „	..	—	—	34·5
				(Pipe)
6.30 „	..	13·4	—	26·4
7 „	..	—	12·5	34·3

After this training was completed we tested, on different days, the accuracy of the localization of tactile stimuli for the "trained" spots on the palmar aspect of the right index finger at different intervals of time throughout the day. Table XI gives the results obtained on three occasions—the intervals between tests being four hours, three hours, and half hours respectively. It will be seen that there is no marked progressive change in accuracy during the day—except that the answers appear generally to be less accurate in the late evening:—

On the occasion of the half-hourly test the accuracy of localization was tested for the corresponding spots on all four right fingers before and after the experiment. The accuracy seems to be markedly less for the second and third digits after it (Table XII). The accuracy of localization was tested at the same time for the set of "untrained" spots on the palmar aspects of the same fingers (those spots which lay on the folds of skin near the joints). Comparatively little change is seen to occur in the case of the second and third digits: but there is a curious reversal of degree of accuracy in the case of the fourth and fifth:—

TABLE XII.—"AVERAGE ERROR PER CENT." OF LOCALIZATION OF THE SPOTS ON THE PALMAR ASPECTS OF ALL THE FOUR RIGHT DIGITS BEFORE AND AFTER THE RECORDS GIVEN IN THE THIRD COLUMN OF TABLE II.

Finger		Before		After
Palmar L 3	..	13.9	..	0.0
R 2	..	7.6	..	34.3
R 3	..	18.8	..	29.2
R 4	..	43.0	..	47.7
R 5	..	43.9	..	31.7

"AVERAGE ERROR PER CENT." FOR THE "UNTRAINED" SPOTS ON THE PALMAR ASPECTS OF THE SAME FINGERS BEFORE AND AFTER THESE RECORDS.

Finger		Before		After
Palmar L 3	..	18.0	..	4.8
R 2	..	60.0	..	65.3
R 3	..	37.6	..	35.2
R 4	..	28.7	..	55.6
R 5	..	50.8	..	7.6

On the three mornings of the days which immediately followed each of these three trainings the accuracy of localization was tested for the dorsal and palmar sets of spots of all the fingers used in the experiments (Table XIII).

There was a very slight progressive increase in the accuracy of localization of the trained spots of the right index finger; but no regular change in the case of the spots on the back of it, nor in the case of the palmar or dorsal sets of spots on any of the other fingers.

TABLE XIII.—“AVERAGE ERROR PER CENT.” OF LOCALIZATION OF THE SPOTS ON THE PALMAR AND DORSAL ASPECTS OF EACH FINGER ON THE THREE DAYS, EACH OF WHICH IMMEDIATELY SUCCEEDED A “TRAINING” OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX FINGER. EACH FIGURE CALCULATED FROM TWENTY-FIVE OBSERVATIONS.

Finger		DAY OF EXPERIMENT.		
		6	7	8
Palmar	L 3	.. 8.5	.. 0.0	.. 4.2
	L 4	.. 0.0	.. 0.0	.. 0.0
	R 2	.. 39.7	.. 37.2	.. 32.6
	R 3	.. 46.3	.. 42.9	.. 46.6
	R 4	.. 42.0	.. 50.0	.. 37.0
Dorsal	R 5	.. 21.1	.. 57.2	.. 27.8
	L 3	.. 3.7	.. 0.0	.. 0.0
	L 4	.. 0.0	.. 0.0	.. 0.0
	R 2	.. 28.0	.. 13.1	.. 37.6
	R 3	.. 31.2	.. 3.7	.. 35.4
	R 4	.. 32.9	.. 26.7	.. 32.8
	R 5	.. 18.8	.. 25.6	.. 39.3

(4) *On the Records which were taken during the Five Days which immediately succeeded the first Period of Training.*

The ordinary tests were continued on the five days which immediately followed the first attempted training in this experiment. The general results obtained on these days are given in the following table (XIV), where they are expressed as “average error per cent.”:—

TABLE XIV.—“AVERAGE ERROR PER CENT.” FOR LOCALIZATION OF TACTILE STIMULI ON THE PALMAR AND DORSAL SETS OF SPOTS OF EACH FINGER ON EACH OF THE FIVE DAYS IMMEDIATELY SUCCEEDING THE FIRST ATTEMPT TO TRAIN THE PALMAR SPOTS OF THE RIGHT INDEX FINGER. EACH FIGURE (EXCEPT THE AVERAGES AND MEAN VARIATIONS IN THE RIGHT-HAND COLUMNS) IS CALCULATED FROM TWENTY-FIVE OBSERVATIONS—SAVE THE FIGURES FOR THE PALMAR SET OF SPOTS ON THE TRAINED RIGHT INDEX FINGER, WHICH ARE CALCULATED FROM FIFTY OBSERVATIONS.

Finger		DAY OF EXPERIMENT.					Average	Mean variations
		9	10	11	12	13		
Palmar	L 3	.. 0.0	.. 0.0	.. 3.3	.. 13.9	.. 0.0	= 3.44	.. 4.18
	L 4	.. 0.0	.. 0.0	.. 3.7	.. 0.0	.. 3.3	= 1.40	.. 1.68
	R 2	.. 16.7	.. 15.1	.. 15.7	.. 7.6	.. 23.5	= 15.72	.. 3.50
	R 3	.. 39.5	.. 6.1	.. 42.7	.. 18.8	.. 41.3	= 29.68	.. 13.78
	R 4	.. 41.8	.. 39.8	.. 42.0	.. 43.0	.. 48.7	= 43.06	.. 2.23
Dorsal	R 5	.. 52.4	.. 26.1	.. 27.0	.. 43.9	.. 54.0	= 40.65	.. 11.30
	L 3	.. 0.0	.. 12.5	.. 8.9	.. 6.6	.. 3.7	= 6.34	.. 3.59
	L 4	.. 0.0	.. 0.0	.. 11.1	.. 16.9	.. 0.0	= 5.60	.. 6.72
	R 2	.. 12.2	.. 35.3	.. 27.3	.. 15.6	.. 17.7	= 21.62	.. 7.74
	R 3	.. 7.5	.. 0.0	.. 14.7	.. 19.4	.. 37.0	= 15.72	.. 9.98
	R 4	.. 15.9	.. 32.4	.. 12.6	.. 7.9	.. 34.4	= 20.64	.. 10.21
	R 5	.. 14.4	.. 28.3	.. 28.0	.. 11.1	.. 29.0	= 22.16	.. 7.53

The differences between these results and the corresponding ones which were taken before the "training" of the palmar spots of the right index finger will be discussed later. We may, however, note here that of the spots on the palmar aspects of the four fingers of the right hand those of the right index finger are now considerably the most accurately localized. In order of decreasing accuracy of localization of tactile stimuli these fingers are now arranged thus: R 2, R 3, R 5, R 4: whereas before the training of the right index finger ("R 2") that order was: R 3, R 2, R 5, R 4. But when the accuracy of localization is examined for the dorsal aspects of the same fingers they are arranged in order of decreasing accuracy of localization thus: R 3, R 4, R 2, R 5; that is, in exactly the same order as before the training.

When the figures for the palmar set of spots on the right index finger ("R 2"—the "trained" finger) are examined it is seen that there is a gradual decrease in average percentage error as the records proceed—except in the case of the test taken on the thirteenth day of the experiment. The conditions on that occasion were perhaps peculiar. The subject had spent a comparatively sleepless night, and on the following day he was too unwell to complete the tests. We have included this thirteenth record in our series, but the fourteenth is excluded as it is not a complete one.

In the next table (XV) the analysis of error of localization is given for the three individual spots in all the five records.

TABLE XV.—THE TOTAL PERCENTAGE ERROR OF LOCALIZATION FOR EACH OF SPOTS "1," "2," AND "3" ON THE PALMAR AND DORSAL ASPECTS OF EACH OF THE FINGERS EXAMINED ON THE FIVE DAYS WHICH IMMEDIATELY FOLLOWED UPON THE TRAINING OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX FINGER. EACH PERCENTAGE IS CALCULATED FROM ABOUT FORTY-TWO OBSERVATIONS, EXCEPT THE PERCENTAGES FOR THE SPOTS ON THE PALMAR ASPECT OF THE RIGHT INDEX FINGER (R2) WHICH ARE CALCULATED FROM ABOUT EIGHTY-THREE.

Finger		Spot		
		1	2	3
Palmar	L 3	0·00	4·35	6·82
	L 4	0·00	4·55	0·00
	R 2	0·00	20·99	26·53
	R 3	14·29	35·42	40·48
	R 4	15·38	42·50	69·57
Dorsal	R 5	39·53	41·46	36·59
	L 3	8·82	6·12	2·38
	L 4	11·63	4·55	0·00
	R 2	31·03	10·20	23·40
	R 3	25·71	8·33	14·29
	R 4	30·77	20·51	10·64
	R 5	41·86	11·90	7·50

The number of observations from which the percentages are calculated in the case of the spots on the palmar surface of the right index finger ("trained") is double that in the case of the other fingers—i.e., a total of 250 observations for the three palmar spots of the right index finger as against 125 observations for the palmar spots of each of the other fingers, and for each of the dorsal sets of spots on all the fingers.

The most remarkable feature of this table is the entire absence of error of localization in the case of the spot on the palmar aspect of the terminal phalanx of the trained right index finger—that is, spot "1"; and the very great reduction of error in the case of the other two spots on the palmar aspect of that finger, as compared with the records before training. In the case of spot "1" no error of localization occurred at any of seventy-one observations distributed over the five different days. A comparison of this table with Table II is extremely instructive, but will be deferred to a later sub-section of this paper. It may, however, be pointed out here that in the case of the palmar sets of spots on the other three fingers there is a considerable similarity between the results obtained before and after the training. On the whole there is a small decrease in the error of localization of tactile stimuli; but if the order of accuracy is examined for the three palmar spots of each of the third, fourth, and fifth digits, it is found that it is the same before and after the training of the second digit—save only that in the case of the fifth digit, while spot "2" is still the least accurately localized, after the training spot "3" is the most accurately localized, while before it spot "1" was. More variation of the order of accuracy occurs in the case of the spots on the dorsal aspects of the fingers; but it will be observed that here, as before the training of the palmar set of spots on the right index finger, upon the whole spot "1" (that on the terminal phalanx) is the least accurately localized; while spot "3" (that on the basal phalanx) is the most accurately localized—the reverse of the findings in the case of the palmar spots.

It will be remembered that in the case of spot "3" on the palmar aspect of the fourth right digit, the error of localization was found to be greater than that which would have been expected to be given had the answers been selected by hazard. The error of hazard should here be 66·67 per cent.; and it will be seen that the error of localization for that spot on that finger is still greater than the hazard error, but yet not so great as before the training of the second digit. It is a matter of interest to examine this error again, and to compare it with the error for the same spot in the first series of records.

In Table III—column B—the percentages of error of localization for this spot on each of the five records taken after the training of the right index finger are given. And on Table IV—column B—there is an analysis of the total number of answers given for this spot in these records. When columns A and B are compared in that Table IV, it is seen that after the training (column B) the percentage of right localizations of that spot is about half as great again as the percentage before the training of the right index finger. On the other hand, the percentages for the wrong answers spot “1” and spot “2” are almost exactly the same as before. The increase in the number of right answers after the training of the other finger seems to have occurred at the expense of the “confused” answers which were given before the training. In other words, the subject now never says that he is unable to localize a tactile stimulus applied to this spot; but when he makes a wrong localization the percentage error for the wrong answer is the same as before. In this case the error of hazard would be 25 per cent.—or 33·33 per cent. if the answer “confused” be regarded as now eliminated from the possibilities. And yet the wrong answer spot “2” is given on 66·67 per cent. of occasions. There is, therefore, here a very definite “positive error” which cannot be explained by the mere taking away of a cortical function, but is rather to be looked upon as conditioned by a distortion of a cortical function. Into this question of “positive error” we shall inquire later.

In the records taken on the five days after the training of the right index finger, the state of “confusion” in answer to tactile stimuli practically disappeared. That is to say, that the subject scarcely ever indicated that he was unable to localize a stimulus.

In the following table (Table XVI) the figures for the localization by the subject of two consecutive similarly located stimuli upon two different spots are given as percentages of the number of times two such similar consecutive stimuli were applied. On comparison with the corresponding Table VI (for the figures before the training of the palmar spots on the right index finger) it will be seen that there is a considerable fall in the average error for spots on the palmar aspect of the right index finger; a considerably smaller fall in the case of these spots on the fourth right digit; little change in the case of the third right digit; and a considerable rise in that of the fifth. There is an even greater fall in this error in the case of the dorsal set of spots on the right index finger.

TABLE XVI.—THE PERCENTAGE NUMBER OF TIMES PAIRS OF TWO CONSECUTIVE SIMILARLY LOCATED STIMULI WERE LOCALIZED ON TWO DIFFERENT SPOTS; GIVEN FOR EACH ASPECT OF EACH FINGER ON THE FIVE DAYS WHICH IMMEDIATELY SUCCEEDED THE TRAINING OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX FINGER, AND EXPRESSED AS PERCENTAGES OF THE NUMBER OF TIMES TWO SIMILARLY LOCATED STIMULI WERE GIVEN CONSECUTIVELY.

		DAY OF EXPERIMENT					Average	Mean variation
Finger		9	10	11	12	13		
Palmar	L 3	.. 0.0	.. 0.0	.. 16.7	.. 0.0	.. 0.0	= 3.3	.. 5.3
	L 4	.. 0.0	.. 0.0	.. 14.3	.. 0.0	.. 11.1	= 5.1	.. 6.1
	R 2	.. 7.7	.. 15.4	.. 25.0	.. 16.7	.. 25.0	= 18.0	.. 5.6
	R 3	.. 66.7	.. 0.0	.. 50.0	.. 0.0	.. 50.0	= 33.3	.. 26.7
	R 4	.. 20.0	.. 0.0	.. 50.0	.. 0.0	.. 50.0	= 24.0	.. 20.8
	R 5	.. 50.0	.. 25.0	.. 60.0	.. 100.0	.. 55.6	= 58.1	.. 17.5
Dorsal	L 3	.. 0.0	.. 12.5	.. 33.3	.. 0.0	.. 12.5	= 11.7	.. 9.3
	L 4	.. 0.0	.. 0.0	.. 0.0	.. 0.0	.. 0.0	= 0.0	.. 0.0
	R 2	.. 0.0	.. 0.0	.. 25.0	.. 16.7	.. 12.5	= 10.8	.. 8.7
	R 3	.. 0.0	.. 0.0	.. 66.7	.. 16.7	.. 75.0	= 31.7	.. 31.3
	R 4	.. 0.0	.. 0.0	.. 33.3	.. 12.5	.. 40.0	= 17.2	.. 15.6
	R 5	.. 14.3	.. 12.5	.. 20.0	.. 16.7	.. 66.7	= 26.0	.. 16.2

In Table XVII the number of times two consecutive differently located spots were localized by the subject upon the same spot are given. A comparison with Table VII shows little change in the figures. Table XVIII gives the corresponding figures for cases in which the first of a pair of consecutive dissimilarly located tactile stimuli was rightly localized by the subject, but the second stimulus wrongly localized by him upon the same spot as the first. A comparison with the corresponding Table VIII (for the records before the training of the palmar spots on the right index finger) again shows little change after the training.

TABLE XVII.—THE NUMBER OF TIMES TWO DIFFERENT CONSECUTIVE STIMULI WERE LOCALIZED UPON THE SAME SPOT—GIVEN FOR THE PALMAR AND DORSAL SETS OF SPOTS ON EACH FINGER ON EACH OF THE FIVE DAYS WHICH IMMEDIATELY SUCCEEDED THE TRAINING OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX FINGER.

		DAY OF EXPERIMENT					Average	Mean variation
Finger		9	10	11	12	13		
Palmar	L 3	.. 0	.. 0	.. 0	.. 4	.. 0	= 0.8	.. 1.28
	L 4	.. 0	.. 0	.. 1	.. 0	.. 0	= 0.2	.. 0.32
	R 2	.. 5	.. 5	.. 3	.. 1	.. 6	= 4.0	.. 1.60
	R 3	.. 7	.. 2	.. 7	.. 1	.. 10	= 5.4	.. 3.12
	R 4	.. 9	.. 7	.. 2	.. 4	.. 6	= 5.6	.. 2.08
	R 5	.. 5	.. 4	.. 2	.. 7	.. 6	= 4.8	.. 1.44
Dorsal	L 3	.. 0	.. 1	.. 0	.. 2	.. 1	= 0.8	.. 0.64
	L 4	.. 0	.. 0	.. 3	.. 3	.. 0	= 1.2	.. 1.44
	R 2	.. 4	.. 7	.. 2	.. 2	.. 3	= 3.6	.. 1.52
	R 3	.. 1	.. 0	.. 3	.. 4	.. 7	= 3.0	.. 2.00
	R 4	.. 5	.. 5	.. 2	.. 2	.. 8	= 4.4	.. 1.92
	R 5	.. 2	.. 4	.. 3	.. 3	.. 4	= 3.2	.. 0.64

TABLE XVIII.—THE NUMBER OF TIMES THE SECOND OF A PAIR OF DISSIMILAR CONSECUTIVE STIMULI WAS WRONGLY LOCALIZED ON THE SAME SPOT AS THAT ON WHICH THE FIRST OF THE PAIR HAD BEEN CORRECTLY LOCALIZED—GIVEN FOR THE PALMAR AND DORSAL SETS OF SPOTS ON EACH FINGER ON EACH OF THE FIVE DAYS WHICH IMMEDIATELY SUCCEEDED THE TRAINING OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX FINGER. (IN THE CASE OF EACH RECORD FOR EACH FINGER, SAVE THAT FOR THE PALMAR ASPECT OF THE RIGHT INDEX FINGER—"R₂"—THERE WERE ABOUT TWENTY PAIRS OF DISSIMILAR STIMULI GIVEN; IN THE CASE OF "R₂" ABOUT FORTY PAIRS WERE GIVEN, AND THE NUMBER OF ERRORS FOR THAT FINGER HAS HERE BEEN DIVIDED BY TWO.)

Finger	DAY OF EXPERIMENT.					Average	Mean variation
	9	10	11	12	13		
Palmar L 3 ..	0 ..	0 ..	0 ..	2 ..	0 ..	0.4 =	0.64 ..
L 4 ..	0 ..	0 ..	1 ..	0 ..	0 ..	0 =	0.32 ..
R 2 ..	2.5 ..	2.5 ..	1.0 ..	0.5 ..	4.5 ..	2.2 =	1.16 ..
R 3 ..	3 ..	1 ..	1 ..	0 ..	6 ..	2.2 =	1.84 ..
R 4 ..	5 ..	4 ..	1 ..	2 ..	3 ..	3.0 =	1.20 ..
R 5 ..	3 ..	2 ..	0 ..	5 ..	4 ..	2.8 =	1.44 ..
Dorsal L 3 ..	0 ..	1 ..	0 ..	1 ..	0 ..	0.4 =	0.48 ..
L 4 ..	0 ..	0 ..	2 ..	2 ..	0 ..	0.8 =	0.96 ..
R 2 ..	3 ..	4 ..	1 ..	2 ..	1 ..	2.2 =	1.04 ..
R 3 ..	1 ..	0 ..	2 ..	2 ..	5 ..	2.0 =	1.20 ..
R 4 ..	4 ..	3 ..	0 ..	2 ..	5 ..	2.8 =	1.44 ..
R 5 ..	2 ..	3 ..	2 ..	2 ..	3 ..	2.4 =	0.48 ..

A comparison of Tables XVI and XVIII seems to show that there is little or no regular relationship between the rates of incidence of these two types of error (one associated with defect of "individuality," the other with defect of "character") in the different fingers on the different days. Both errors may be relatively high in a certain finger, and relatively low in another; while, in yet another finger—or on another occasion—one error may be relatively high, and the other relatively low. But a comparison of the corresponding figures for these errors before the training of the palmar set of spots on the right index finger seems to hint that then there was an indication of a relationship between the two types of error. For when the incidence of one of the types of error is relatively high in a certain finger on a certain day, often the incidence of the other of the types of error in that finger on that day is relatively low (Tables VI, VIII).

(5) *On the Effect of the "training" of the Palmar Set of Spots on the right Index Finger; comparison of the Records before and after it.*

With regard to the effect of the training of the palmar sets of spots on the right index finger, three questions arise. In the first place, did an improvement in the accuracy of the localization of tactile stimuli upon these spots occur after the training, and was this improvement

markedly greater than any which may have occurred in the case of any of the other sets of spots examined in these experiments?

In the second place, provided such an improvement occurred, is it possible to refer it to any definite factors (such as, improvement in the "character" of the spots, improvement in their "individualities," "improvement in their positions"), and does this give us any information with regard to the initial state of badness of localization of tactile stimuli?

And, thirdly, what are the restrictions of the improvement, that is, can it be shown to occur in the case of sets of spots other than the trained ones, or is it confined to these?

Now, there is no doubt that a very definite and striking improvement in the accuracy of localization of tactile stimuli occurred in the case of the "trained" spots on the palmar aspect of the right index finger; and that no such great improvement occurred in the case of any other set of spots.

Table XIX sufficiently demonstrates this. In that table there is given side by side the average per record of the "average error per cent" of localization of tactile stimuli on the palmar and dorsal aspects of each of the fingers, in the first place before the training and in the second place after it.

TABLE XIX.—COMPARISON OF THE ERRORS OF LOCALIZATION ON THE DIFFERENT FINGERS FOR: A, THE FIVE DAYS IMMEDIATELY PRECEDING; AND B, THE FIVE DAYS IMMEDIATELY SUCCEEDING THE TRAINING OF THE SPOTS ON THE PALMAR ASPECT OF THE RIGHT INDEX FINGER—EXPRESSED AS THE AVERAGE PER RECORD OF THE "AVERAGE ERRORS PER CENT."; IN COLUMN C THE DIFFERENCE BETWEEN THE TWO AVERAGES IS EXPRESSED AS A PERCENTAGE OF THE FIRST.

		A.				B.				C.	
Finger		Average		m.v.		Average		m.v.		Difference of averages	
Palmar	L. 3	..	1.48	..	2.37	..	3.44	..	4.18	..	+ 1.96
	L. 4	..	4.52	..	5.42	..	1.40	..	1.68	..	- 3.12
	R. 2	..	42.70	..	3.80	..	15.72	..	3.50	..	- 26.98
	R. 3	..	31.98	..	8.30	..	29.68	..	13.78	..	- 2.30
	R. 4	..	46.72	..	5.96	..	43.06	..	2.23	..	- 3.66
	R. 5	..	43.06	..	6.37	..	40.68	..	11.30	..	- 2.38
Dorsal	L. 3	..	0.66	..	1.06	..	6.34	..	3.59	..	+ 6.34
	L. 4	..	2.04	..	1.63	..	5.60	..	6.72	..	+ 3.56
	R. 2	..	28.56	..	7.19	..	21.62	..	7.74	..	- 6.94
	R. 3	..	18.76	..	2.94	..	15.72	..	9.98	..	- 2.04
	R. 4	..	26.80	..	8.40	..	20.64	..	10.21	..	- 6.16
	R. 5	..	32.62	..	9.22	..	22.16	..	7.53	..	- 10.46

It will be seen that there is a very marked fall (from 42.70 per cent. to 15.72 per cent.) in the error for the palmar spots of the right index

finger ("R 2") after the training of them. The difference of these two percentages is about 27; and, although there is a slight improvement in the case of the spots on the palmar aspects of the other fingers of the right hand, the difference of the percentages of the finger which shows the greatest improvement after the index finger (the fourth digit) is less than 4. Reckoned as percentages of the larger percentage (that before the training) these differences would be about 63·2 per cent. and 7·8 per cent. respectively. This therefore demonstrates a very great improvement of localization of tactile stimuli on the palmar set of spots of the right index finger, and a slight improvement on these spots of the other fingers of the right hand.

When the figures for the sets of spots on the dorsal aspects of the right fingers are examined, it is seen that in every case an improvement of localization of tactile stimuli has occurred. The greatest improvement occurs in the case of the little finger, but the difference between the two percentages there is 10—about 32 per cent. of the figure before the training of the palmar spots on the index finger.

A great improvement of the localization of tactile stimuli on the three palmar spots of the right index finger therefore occurred—in what did it consist? It is possible to examine here the error for each of the three spots separately, and to examine the kinds of error which were made before and after the training.

Now with regard to the error for each of the three spots—in the following table (Table XX) the total number of times the four possible answers were given in reply to tactile stimuli, applied to each spot of each aspect of the fingers of the right hand, is expressed as a percentage of the total number of times each spot was touched in the tests before and after the training of the palmar set of spots on the right index finger.

Obviously, if the subject knows that the spot touched is one of three possible ones there are four possible answers to each tactile stimulus—that is, "It is on spot 1," spot "2," or spot "3," while the fourth answer is "I cannot decide"—which we may call "confusion." Of the answers spot "1," spot "2," and spot "3" one is right for each spot the tactile stimulus is located upon; in the table the figures for the right answer to each spot are emphasized.

We notice at once that in the case of the right index finger (palmar aspect), whereas the localization of spot "1" was right on 66·67 per cent. of occasions before the training, after the training the percentage rises to 100—no mistakes were made. The difference between these

percentages is about 33. When we examine the figures for the corresponding spot ("1"—the spot on the terminal phalanx) on the palmar aspects of the other fingers of the right hand, and on the dorsal aspects of all the right fingers, we find that in the case of this spot on the palmar aspect of the fourth digit and on the dorsal aspects of the second and fourth digits there is also an improvement. But it is comparatively slight—the difference of the percentages in the case of the greatest of these improvements being about 15. In all the other cases the localization of tactile stimuli upon spot "1" is worse after the training of the right index finger.

TABLE XX.—THE AVERAGE PERCENTAGE PER RECORD OF THE DIFFERENT ANSWERS ("SPOT 1," "SPOT 2," "SPOT 3," AND "CONFUSED") GIVEN TO THE TACTILE STIMULI APPLIED TO EACH OF THE THREE SPOTS ON EACH ASPECT OF EACH FINGER: A, IN THE FIVE RECORDS BEFORE THE TRAINING OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX-FINGER; AND B, IN THE FIVE RECORDS AFTER THAT TRAINING.

Finger	Spot	A. BEFORE. Answers				B. AFTER, Answers			
		"1"	"2"	"3"	"Con."	"1"	"2"	"3"	"Con."
Palmar R. 2	1	67.57	18.92	5.41	8.11	100.00	0.00	0.00	0.00
	2	10.42	37.50	27.08	25.00	2.47	79.01	18.51	0.00
	3	5.00	20.00	65.00	10.00	2.04	24.49	73.47	0.00
R. 3	1	86.67	8.89	0.00	4.44	85.71	11.43	2.86	0.00
	2	7.89	73.68	7.89	10.53	14.58	64.58	20.83	0.00
	3	4.76	47.62	40.47	7.14	4.76	35.71	59.52	0.00
R. 4	1	74.29	14.29	2.86	8.57	84.62	7.69	7.69	0.00
	2	7.84	68.63	11.76	11.76	10.00	57.50	30.00	2.50
	3	2.56	66.67	20.51	10.26	4.35	65.22	30.43	0.00
R. 5	1	62.22	17.78	15.56	4.44	60.46	34.88	4.65	0.00
	2	2.22	53.33	28.89	15.56	21.95	58.54	19.51	0.00
	3	5.71	31.43	60.00	2.86	0.00	34.15	63.41	2.44
Dorsal R. 2	1	54.05	18.92	5.41	21.62	68.97	27.59	3.45	0.00
	2	0.00	75.00	18.75	6.25	6.12	89.80	4.08	0.00
	3	0.00	7.50	85.00	7.50	2.13	21.28	76.60	0.00
R. 3	1	84.44	2.22	0.00	3.33	74.29	20.00	5.71	0.00
	2	5.26	65.79	15.79	13.16	4.17	91.67	4.17	0.00
	3	2.38	4.76	92.86	0.00	0.00	14.29	85.71	0.00
R. 4	1	68.57	8.57	5.71	17.14	69.23	28.21	2.56	0.00
	2	9.80	68.63	13.73	7.84	7.69	79.49	12.82	0.00
	3	7.69	10.26	79.49	2.56	4.26	6.38	89.36	0.00
R. 5	1	62.22	17.78	6.67	13.33	58.14	30.23	11.63	0.00
	2	20.00	60.00	4.44	15.56	4.76	88.10	7.14	0.00
	3	2.86	5.71	82.86	8.57	5.00	2.50	92.50	0.00

In the case of spot "2" (that on the middle phalanx) a yet greater relative improvement occurs on the right index finger—but error here does not disappear after the training. In the case of no other finger does improvement of localization of the corresponding spot proceed to

such a great extent; and in the case of the palmar aspects of the fingers other than the index finger improvement occurs only in the case of spot "2" on the fifth digit—and there the difference in the percentages is only about 5, whereas in the case of the index finger it is about 42.

In the case of the localization on spot "3" of the palmar aspect of the right index finger (the spot on the basal phalanx) a slight improvement occurs. A similar improvement also takes place in the case of the corresponding spot on the palmar aspects of the third, fourth, and fifth digits (in the case of the third and fourth digits being much greater than the improvement in the case of the trained index finger) and on the dorsal aspects of the fourth and fifth digits (the improvement there being also slightly greater than that in the case of the palmar aspect of the right index finger); the localization of spot "3" on the dorsal aspects of the right second and third digits is worse after the training of the palmar set of spots on the index finger.

It may perhaps be inferred that the improvement of the accuracy of localization of tactile stimuli upon spot "3" on the palmar and dorsal aspects of all the fingers is a more or less general one; but that the great improvement of localization on spots "1" and "2" on the palmar aspect of the right index finger is a special one conditioned by the training given to that set of spots on this finger.

When the answers for the palmar aspects of the right index finger are examined, it is seen at once that "confusion" disappears after the training. In the case of tactile stimuli applied to spot "1" the wrong answers spot "2" and spot "3" also disappear; but in the case of spot "2"—while "confusion" does not occur after the training—the wrong answers spot "1" and spot "3" are only reduced. The reduction is, however, large and the increase in the accuracy of the localization of stimuli applied to this spot may perhaps be looked upon as conditioned by the absence of confusion—the decision now being made in the right direction, and by the reduction of the wrong replies. When the answers to spot "3" are examined it is seen that the wrong reply spot "1" is given slightly less often after the training, and the wrong reply spot "2" slightly more often. These differences are small, and the increase in the proportion of right answers may perhaps be looked upon as conditioned by the absence of confusion—as it were the decision being now made, and in the right direction. It will be seen that "confusion" practically disappears for all the fingers after the training of the right index finger; but it is by no means the case that the

improvement of the accuracy of localization of a spot is greatest where the proportion of "confusion" answers was greatest before the training of the right index finger.

An interesting point is exhibited by this table. Where, before the training of the right index finger, the proportion of confusion answers is great for all the fingers the proportion of each answer to each spot should have been about 25 per cent. had the answers been selected by hazard. After the training of the index finger it is perhaps fairer to assume that, as "confusion" practically disappears for all the fingers, the hazard proportion should have been about 33.3 per cent. for each answer. Now, when the table is examined, it is seen that in the case of several answers the proportion is greater than that of hazard. Except in the case of the right answer to spot "3" on the palmar aspect of the fourth right digit both before and after training of the index finger, this is uniformly so both before and after the training for the correct answers to each spot on each aspect of each finger. In other words, there is almost uniformly a positive bias in the direction of the correct answer. But when the incorrect answers are examined it is seen that in certain cases there is an error greater than the error of hazard. (Finger R 2—answer spot "3" to stimuli on spot "2"; R 3—spot "2" to spot "3"; R 4—spot "2" to spot "3"; R 5—spot "3" to spot "2," and spot "2" to spot "3"—all on the palmar aspects of the fingers, no instance on the dorsal, before training; and R 3—answer spot "2" to stimuli on spot "3"; R 4—spot "3" to spot "2," and spot "2" to spot "3"; R 5 spot "1," spot "2" to spot "3"—all on the palmar aspects of the fingers after training, and, perhaps, R 2—answer spot "2" to stimuli on spot "1"; R 4—spot "2" to spot "1"; R 5—spot "2" to spot "1"—all on the dorsal aspects of the fingers after training of the spots on the palmar aspect of the index-finger). In the case of stimuli applied to spots "2" and "3" on the palmar aspects of the fingers there seems to be a fairly definite incorrect identification of "2" with "3" and "3" with "2." In the case of the dorsal sets of spots there is, after the training of the palmar set of spots on the right index finger, a most curious increase of the mistake of localizing stimuli which were applied to spot "1" upon spot "2"—and this is the case for all the fingers. After the training of the palmar spots of the index finger this mistake becomes positive—greater than the error of hazard.

Before we leave this table it may be noticed that in the case of the answer spot "1" this error diminishes for spots "2" and "3" on the

palmar aspect of the right index finger (trained) along with the increase of accuracy of localizing stimuli applied to spot "1" itself; but there is no corresponding decrease in this error for spots "2" and "3" in the case of the other fingers (except perhaps in the case of spot "3" on the little finger) and no corresponding increase of accuracy of the localization of spot "1" on these fingers. From this it would appear that the effect of the training is not spread over the other fingers—but we shall return to this question later.

In Table XXI the average number of times two consecutive similarly situated stimuli were localized upon different spots is given for the records before and after the training of the palmar spots on the right index finger. It will be seen that a considerable decrease in this form of error took place in the case of the palmar and dorsal sets of spots on the right index finger; that a considerable decrease took place for the dorsal set of spots on the little finger; and that a great increase occurred in the case of the palmar spots of the little finger. In the other instances the variation is probably negligible.

TABLE XXI.—COMPARISON OF THE AVERAGE NUMBER OF TIMES PER. CENT. PER RECORD THAT PAIRS OF TWO CONSECUTIVE SIMILARLY SITUATED STIMULI WERE LOCALIZED UPON TWO DIFFERENT SPOTS: A, BEFORE THE TRAINING OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX FINGER; AND B, AFTER THAT TRAINING.

		A				B					
Finger		Average		m.v.		Average		m.v.		Difference of averages	
Palmar	L. 3	..	8.0	..	12.8	..	3.3	..	5.3	..	- 4.7
	L. 4	..	5.0	..	8.0	..	5.1	..	6.1	..	+ 0.1
	R. 2	..	40.0	..	16.0	..	18.0	..	5.6	..	- 22.0
	R. 3	..	34.5	..	19.6	..	33.3	..	26.7	..	- 1.2
	R. 4	..	32.3	..	7.9	..	24.0	..	20.8	..	- 8.0
Dorsal	R. 5	..	28.3	..	12.8	..	58.1	..	17.5	..	+ 29.8
	L. 3	..	2.9	..	4.6	..	11.7	..	9.3	..	+ 8.8
	L. 4	..	7.5	..	9.0	..	0.0	..	0.0	..	- 7.5
	R. 2	..	38.0	..	17.6	..	10.8	..	8.7	..	- 27.2
	R. 3	..	23.8	..	12.4	..	31.7	..	31.3	..	+ 7.9
	R. 4	..	25.5	..	1.37	..	17.2	..	15.6	..	- 8.3
	R. 5	..	48.3	..	24.2	..	26.0	..	16.2	..	- 22.3

The chief point of interest is that here the improvement of this error in the case of the right index finger applies not only to the trained spots on the palmar aspect but also to the untrained ones on the dorsal aspect.

In Tables XXII and XXIII the errors in which the same answer was given to two consecutive stimuli which were situated on different spots are compared for the records before and after the training of the palmar spots on the right index finger—in the second table the figures apply

only to those errors in which the first spot was correctly localized and the second incorrectly, on the same spot as the first. It is seen that, although this error decreases for the palmar spots of the right index finger, the decrease is not so great as that in the case of some of the other fingers.

TABLE XXII.—COMPARISON OF THE AVERAGE NUMBER OF TIMES PER RECORD TWO DIFFERENT CONSECUTIVE STIMULI WERE LOCALIZED UPON THE SAME SPOT: A, BEFORE THE TRAINING OF THE PALMAR SET OF SPOTS, ON THE RIGHT INDEX FINGER; AND B, AFTER THAT TRAINING.

Finger	A			B			Difference of averages
	Average number	m.v.		Average number	m.v.		
Palmar L. 3	0.0	0.0	..	0.8	1.28	..	+ 0.8
L. 4	0.8	0.96	..	0.2	0.32	..	- 0.6
R. 2	5.4	2.5	..	4.0	1.60	..	- 1.4
R. 3	4.8	1.4	..	5.4	3.12	..	+ 0.6
R. 4	5.6	2.1	..	5.6	2.08 0.0
R. 5	6.8	1.8	..	4.8	1.44	..	- 2.0
Dorsal L. 3	0.0	0.0	..	0.8	0.64	..	+ 0.8
L. 4	0.8	0.6	..	1.2	1.44	..	+ 0.4
R. 2	3.8	0.6	..	3.6	1.52	..	- 0.2
R. 3	3.4	1.9	..	3.0	2.00	..	- 0.4
R. 4	4.2	1.5	..	4.4	1.92	..	+ 0.2
R. 5	4.4	1.1	..	3.2	0.64	..	- 1.2

TABLE XXIII.—COMPARISON OF THE AVERAGE NUMBER OF TIMES PER RECORD THE SECOND OF A PAIR OF CONSECUTIVE DISSIMILAR STIMULI WAS WRONGLY LOCALIZED UPON THE SAME SPOT AS THAT ON WHICH THE FIRST STIMULUS HAD BEEN CORRECTLY LOCALIZED: A, BEFORE THE TRAINING OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX FINGER; AND B, AFTER THAT TRAINING.

Finger	A			B			Difference of averages
	Average number	m.v.		Average number	m.v.		
L. 3	0.4	0.64	..	0.4	0.64 0.0
L. 4	0.2	0.32	..	0.2	0.32 0.0
R. 2	2.4	0.96	..	2.2	1.16	..	- 0.2
R. 3	2.8	0.64	..	2.2	1.84	..	- 0.6
R. 4	2.6	1.52	..	3.0	1.20	..	+ 0.4
R. 5	3.6	1.12	..	2.8	1.44	..	- 0.8
Dorsal L. 3	0.0	0.00	..	0.4	0.48	..	+ 0.4
L. 4	0.6	0.48	..	0.8	0.96	..	+ 0.2
R. 2	2.0	0.80	..	2.2	1.04	..	+ 0.2
R. 3	1.8	1.04	..	2.0	1.20	..	+ 0.2
R. 4	2.0	0.80	..	2.8	1.44	..	+ 0.8
R. 5	2.6	0.88	..	2.4	0.48	..	- 0.2

It is interesting to compare Table XXIII with Table XXI. It is then seen that there is little correspondence between the two kinds of error. For a set of spots on one finger both errors may fall after the training; or both may rise; or one may rise and the other may fall.

Before we pass to the consideration of these results one more analysis may be given—that of the occurrence of “dilemma” before and after the training of the index finger. The observation of this phenomena depends very largely upon the experimenter, and the figures here are given with this reservation—for it is extremely difficult to determine in what the dilemma consists. In our experiments the subject pointed with a pencil to the spot on the hand of the model which he supposed to correspond with the spot on his own hand which had just been touched. In doing this he usually placed the point of the pencil directly upon the spot which he wished to indicate. Occasionally the latency of this act was obviously much greater than usual; and then we sometimes counted the answer as one which exhibited “dilemma.” But more usually there was a very distinct indication of the presence of dilemma. The pointer would hover over the spots on the hand of the model—now over one, now over another—and finally the subject would either place the pointer upon one of the spots (in which case we called the answer one characterized by dilemma), or would touch the table in indication that he was unable to locate the tactile stimulus (in which case we called the answer “confusion”). In all these records no word was spoken from beginning to end, and our difficulty was to distinguish “dilemma” from mere delay of response where the pointer did not hover between different spots, and to notice the small indications of this hovering which sometimes occurred. One very marked change occurred after the training of the palmar set of spots on the right index finger, but we had no instruments to record it. The latency of the localizing act of the subject was always very much greater for stimuli applied to the right hand than for those applied to the normal left hand. After the training of the palmar set of spots on the right index finger the latency of their localization was markedly less than that of the localization of tactile stimuli upon the palmar spots of the other fingers; but it never became as small as that of the localization of spots on the left hand.

In the following table (Table XXIV) the number of times dilemma occurred in the five records before the training of the right index finger and in the five records after that training is given. A distinction is drawn between cases of dilemma in which the final answer was wrong and cases in which it was right.

The decrease of this phenomenon after the training of the palmar spots on the right index finger is seen to occur generally for all the sets of spots examined, and not to be greater in the case of the index finger than in the cases of the other fingers. We do not give a more minute

analysis, for our figures give no indication of a relation between the number of times dilemma occurred and the relative accuracy of localization either for the set of spots on a finger or for any one of these spots.

TABLE XXIV.—A COMPARISON OF THE NUMBER OF TIMES "DILEMMA" OCCURRED: A, IN THE RECORDS BEFORE THE TRAINING OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX FINGER; AND B, IN THE RECORDS, AFTER THAT TRAINING. IN THE COLUMNS THE FIRST NUMBER DENOTES THE TIMES THE FINAL RESULT OF THE DILEMMA WAS WRONG, THE SECOND NUMBER THE TIMES THE FINAL RESULT WAS RIGHT, AND THE THIRD GIVES THE TOTAL OF THE TWO.

		A BEFORE			B AFTER		
	Finger	Wrong	Right	Total	Wrong	Right	Total
Palmar	L 3	0	0	0	0	0	0
	L 4	0	1	1	0	0	0
	R 2	3	11	14	3	5.5	8.5
	R 3	3	16	19	0	7	7
	R 4	4	12	16	4	5	9
	R 5	6	9	15	3	2	5
Dorsal	L 3	0	0	0	0	0	0
	L 4	1	1	2	0	4	4
	R 2	5	15	20	2	6	8
	R 3	3	14	17	0	5	5
	R 4	3	22	25	0	6	6
	R 5	1	17	18	0	7	7

We may now summarize the results which were obtained after the training of the palmar set of spots on the right index finger.

In the first place a general improvement of the localization of tactile stimuli occurred for all the sets of spots examined in this experiment. But a much greater improvement occurred in the case of the trained set of spots than in the case of any other set, and we are probably justified in attributing the improvement to the training.

This improvement in the case of the trained palmar set of spots was most marked in the case of spot "1" (on the terminal phalanx) and spot "2" (on the middle phalanx). In the localization of the first of these all error disappeared after the training; in the localization of the second each type of error markedly decreased. In the localization of spot "3" (basal phalanx) little change occurred in the different types of error, save that "confusion" disappeared.

Now this improvement might (on our hypothesis) be due (1) to an improvement in the attribute of character of the trained spots (whereby they are recognized as different amongst themselves); or (2) to an improvement of the attribute of individuality (whereby stimuli applied to a specific spot are recognized as similarly located); or (3) to an

improvement of the attribute of position (whereby the tactile stimulus is referred to a special spot on the surface of the body).

In the early records of the experiment—those taken before the training of the right index finger—there was a great tendency for the answers to run in consecutive series, although the stimuli were applied indifferently to the different spots. This is what would be expected to occur if the attribute of character of the tactile stimuli was lost, or at any rate impaired.

In the training which we gave to the palmar spots on the right index finger, the subject in one part of it especially concentrated his attention on the difference between the tactile stimuli which he could then see being applied to the different spots in an indifferent order.

TABLE XXV.—A COMPARISON OF THE TOTAL NUMBER OF TIMES SERIES OF CONSECUTIVE SIMILAR ANSWERS OF DIFFERENT LENGTHS WERE GIVEN: A, IN THE RECORDS BEFORE THE TRAINING OF THE RIGHT INDEX FINGER; AND B, AFTER THAT TRAINING; THE SECOND COLUMNS GIVE ARBITRARY FIGURES OBTAINED BY MULTIPLYING THE NUMBER OF SERIES IN THE FIRST COLUMNS BY THE NUMBER OF ANSWERS IN THE SERIES (2, 3, 4, &c.). THE FIGURES FOR THE DORSAL SETS OF SPOTS ARE NOT GIVEN.

A.						B.				
		BEFORE						AFTER		
Finger	No. in series	No. of series				No. of series				
R 2	..	2	..	7	..	14	..	7	..	14
		3	..	7	..	21	..	3	..	9
		4					..	1	..	4
		5	..	1	..	5	..	1	..	5
		6								
		7								
		8					..	0.5	..	4
		9	..	1 = 16	9 = 49	..	= 12.5	= 36		
	R 3	..	2	..	7	..	14	..	11	..
		3	..	5	..	15	..	1	..	3
		4	..	1	..	4	..	3	..	12
		5	..	1	..	5	..	2	..	10
		6	..	1 = 15	6 = 44	..	1 = 18	6 = 53		
		7								
R 4	..	2	..	3	..	6	..	11	..	22
		3	..	3	..	9	..	5	..	15
		4	..	3	..	12	..	5	..	20
		5	..	4	..	20	..	1	..	5
		6					..	1	..	6
		7	..	1 = 14	7 = 54	..	= 23	= 68		
		8								
R 5	..	2	..	14	..	28	..	13	..	26
		3	..	3	..	9	..	6	..	18
		4	..	1	..	4	..	2	..	8
		5	..	3	..	15	..			
		6	..	2 = 23	12 = 68	..	1 = 22	6 = 58		

After the training the records show a reduction in the number of such consecutive series of similar answers for the spots on the palmar aspect of the right index finger. In the cases of the third and

fourth right digits an increase in this number occurred—that increase being a considerable one in the case of the fourth. While the number in the case of the fifth digit was practically stationary. The figures are given in Table XXV.

This would seem to demonstrate that one of the initial factors in the subject's badness of localization of tactile stimuli consisted in the impairment of the attribute of "character" of the tactile stimuli—the attribute whereby the subject is conscious that tactile stimuli located upon different spots are, in some manner, dissimilar—and that the effect of the training of the spots on the right index finger was to reduce this error for them, but not (at any rate to the same extent) to reduce this error for the spots on the other fingers. It must, however, be noticed that when these figures are analysed in terms of pairs of dissimilarly located stimuli, the first of which is correctly localized by the subject and the second wrongly upon the same spot as the first, the error is not more greatly diminished for the index fingers than for the others (Table XXIII)—but this is perhaps only a part of the special type of error which we are examining.

It would, therefore, seem that impairment of the attribute of character was one of the factors in the initial condition of the subject's inaccuracy of localization of tactile stimuli, and that this impairment was reduced by training a specific set of spots. But it must be noted that the hypothetical attribute of character may not be eliminated—only impaired; for even in the earliest records there were portions where the answers did not run in series, and where at times the localization of tactile stimuli was accurate.

When the early records are examined it is found that at times series of consecutive similarly located stimuli were localized by the subject upon different spots. At these times the answers, of course, did not run in similar series; and the inference (on our hypothesis) is that this error was conditioned by impairment of the attribute of "individuality" in the localization of tactile stimuli—the attribute whereby the subject knows that tactile stimuli applied to the same spot are in some manner similar to each other.

In a part of our training the subject paid special attention to the similarity between tactile stimuli which he saw being applied in consecutive series to a single spot.

After that training the records show a decrease in this type of error—the localizing of consecutive similarly located stimuli upon dissimilar spots—in the case of the trained spots. But there is also a

decrease in the case of the untrained spots on the back of the trained finger. From this it might be inferred that this attitude is, as it were, common to various sets of spots on a finger; but in the case of the little finger a marked increase of error took place for the palmar set of spots, and a marked decrease for the dorsal, after the training of the index finger. When the palmar sets of spots on the fingers are alone considered, the decrease in this type of error is seen to be much less in the cases of the third and fourth digits than in the case of the trained index finger; while an increase of error occurs in the case of the fifth digit (Table XXI).

It may, perhaps, be inferred that this error decreased after the training of the palmar set of spots on the right index finger for that finger, and not to so great an extent for the palmar sets of spots of the other fingers of the right hand; that this error is conditioned by impairment of the attribute of individuality in the localization of tactile stimuli; and that the training reduced this impairment.

If so, we may regard the original condition of the subject as conditioned in part by impairment of the attribute of character, and in part by impairment of the attribute of individuality.

But for the complete and accurate localization of tactile stimuli there is necessary (on our hypothesis) the attribute of "position." In the subject whose state we examined this attribute can hardly have been lost; for then it would be expected that he would have been unable to localize the tactile stimuli; whereas one of the features of this case was the comparatively small proportion of instances in which he could not locate a stimulus. But there seems to be evidence for a definite distortion of this attribute.

That this is so is shown by the occurrence of "positive error" in the localization of certain spots. The error which he made in the localization of certain spots was greater than the error of hazard. In such a case the subject had three choices (excluding the possible "confusion" answer). One of these was the correct answer, and the other two were incorrect. Now, when these errors are analysed (Table XX, see analysis in text), it is seen that in some cases a certain wrong answer would be given more often than the error of hazard. In such cases a distortion, probably of the attribute of position, must be assumed. That is to say, that in certain instances the subject showed a definite tendency to place a certain specific tactile stimulus upon a certain wrong spot rather than upon a certain other wrong spot. The "position" of the tactile stimulus had in some manner been distorted.

This occurred in the case of one of the wrong answers given to spot "2" on the palmar aspect of the right index finger. That was one of the two trained spots which most definitely showed improvement of localization after the training. In the records taken after the training, this positive error was reduced considerably below the error of hazard, but this reduction was not accompanied by an increase on the other possible wrong localization of this spot. In one of the other cases of positive error which occurred in the other fingers before the training of the right index finger, a reduction below the error of hazard also occurred; but in this case that reduction was accompanied by a marked increase in the other possible error in the localization of that spot.

It may, perhaps, be assumed that part of the initial condition of this subject's inaccuracy of localization of tactile stimuli was due to a distortion of the attribute of position; and that after the training this distortion was reduced for the spots which were trained.

One further point with regard to the analysis of the effects of the training—the question whether it was confined to the trained spots or was seen also in others—may be left over to the following subsection of this paper.

(6) *On the Question whether the Improvement in Accuracy of Localization after Training was confined to the Spots which were trained.*

To a certain extent this question may at once be answered. An apparent general improvement of all the spots on the back and front of the fingers occurred after the training of the palmar set of spots on the right index finger. This apparent general improvement was, however, much less than the special improvement of the trained set of spots.

Now, although such an apparent general improvement took place, it cannot definitely be ascribed to the training of a special set of spots. Thus it is, perhaps, possible that the mere repetition of the test might be accompanied by a general improvement in the subject's responses—even although he was never allowed to know when his replies were right or when they were wrong.

To test the possible general effect of the training we used the following method: A second set of spots was selected on the palmar aspect of each finger. These spots lay on the folds of skin which are situated near the inter-phalangeal and metacarpal-phalangeal joints—whereas the spots of the sets which we used in the daily examinations lay over the middle of the phalanges. The set of spots which were

examined from day to day (and were trained on the right index finger) we may term the "ordinary spots" or the "trained spots"; while the other set of spots, which was examined, but rarely so that there might be little or no effect of practice, we may term the "untrained spots," because no set of them were trained.

We had not thought of selecting these second sets of spots before the commencement of the training of the spots on the right index finger, and so we are unable to compare the average errors for the two sets of spots on each finger before the records were complicated by the training. It is possible that the errors were not the same (or not very nearly the same) for the two sets of spots. In another case, which was in almost every respect similar to that which we now describe, we found that the error of localization of tactile stimuli was distinctly greater for the sets of spots over the joints than for the sets of spots which were placed over the middle of the phalanges—although in this case the subject thought that he could localize the former spots more accurately than the latter. When the localization is carried out in an exactly similar manner on the ordinary subject there is little or no difference in the accuracy of localization of supra-liminal tactile stimuli on these two sets of spots—at any rate, with the instrument which we used.

After the training of the palmar set of "ordinary spots" on the right index finger we examined on three occasions the accuracy of localization for the "untrained spots" on the fingers. Two of these examinations were done on the twelfth day of the experiment, and the third on the thirteenth. The following table gives the average error per cent. of localization:—

TABLE XXVI.—AVERAGE ERROR PER CENT. OF LOCALIZATION ON THE "UNTRAINED" SETS OF SPOTS ON THE PALMAR ASPECTS OF THE FINGERS AFTER THE TRAINING OF THE "ORDINARY" SET OF SPOTS ON THE RIGHT INDEX FINGER.

		DAY OF EXPERIMENT						
Finger		12		12a		13		Average
Palmar	L 3	..	18.0	..	4.8	..	0.0	= 7.6
	L 4	..	13.7	..	3.3	..	7.0	= 8.0
	R 2	..	60.0	..	65.3	..	48.1	= 57.8
	R 4	..	37.6	..	35.2	..	47.3	= 40.0
	R 3	..	28.7	..	55.6	..	41.2	= 41.8
	R 5	..	54.1	..	27.6	..	52.9	= 44.9

A glance at this table shows that the index finger ("R. 2") is actually the worst of the four fingers of the right hand. That is to say that this finger—which at this time, after the training, was the best of the four

as regards the localization of tactile stimuli on the "ordinary" spots—is much the worst for the localization of these stimuli when a strange set of spots is selected for examination. The figures in columns 12 and 13 of this table should be compared with those in the corresponding columns (12 and 13) of Table XIV. The latter figures are those for the "ordinary" spots on the same day. Especially when the figures in the column 13 are examined, it will be seen that there is considerable similarity between them as regards the third, fourth, and fifth digits—but that there is a considerable difference when the figures for the second digit (index finger) are examined. The percentage of error is 23·5 for the "ordinary" spots on that finger, and 48·1 for the "untrained" spots; a still greater difference (7·6 per cent. as against 60 per cent.) occurs in column 12. The column of averages may be compared with those in Table XIX ("ordinary" spots, before and after training of right index finger).

TABLE XXVII.—THE TOTAL PERCENTAGE ERROR OF LOCALIZATION FOR EACH OF SPOTS 1, 2, AND 3 OF THE "UNTRAINED" SETS ON THE PALMAR ASPECTS OF THE FINGERS IN THE THREE RECORDS GIVEN IN TABLE XXVI.

Finger		Spot		
		1	2	3
Palmar L	3	14·9	3·7	0·0
	L 4	7·4	16·7	0·0
	R 2	73·3	50·0	50·0
	R 3	66·7	42·4	11·1
	R 4	45·8	29·6	50·0
	R 5	13·9	66·1	51·2

The next table (Table XXVII) gives the average error of localization for each of the three "untrained" spots on each finger in these three records. The corresponding figures for the "ordinary" spots before training the right index finger are given in Table II, and those after the training in Table XV. A comparison of these two tables with the present one demonstrates scarce a point of resemblance. The incidence of error as regards the distal, intermediate, and proximal spots (spots "1," "2," and "3") seems to have no common basis when the figures for the "ordinary" and "untrained" sets of spots are examined. This strongly suggests that the different sets of spots on the same aspect of the same finger have little or nothing in common. On comparison of the figures for spot "1" on the right index finger in this table and in Table XV it will be observed that in the latter case, after training, error has absolutely disappeared; but in the former case (that is, an "untrained" spot which lies in a corresponding position in its set) the

error is as great as 73·3 per cent., and is greater than that of either of the other spots in the set.

The conclusion from these figures would seem to be that the training of a set of spots on a certain finger, although very definitely reducing the error in the localization of tactile stimuli for the trained set of spots, does not reduce the error for other and untrained sets of spots on the same finger. Arguing from this alone, it might be said that the effect of training is confined to the trained spots, and is extended neither to other spots on the trained finger nor to spots on the other fingers. The apparent increase of accuracy in the localization of tactile stimuli on the "ordinary" spots of the other fingers (as shown by our experiments) might then be supposed to be conditioned merely by the effect of practice.

But in this connection it must be noted that the spots which exhibited an increase of accuracy of localization on the other fingers lay in corresponding positions to the trained spots on the right index finger. It might be that the training of the spots on the right index finger was accompanied by a slight increase in accuracy of localization for the corresponding spots on the other fingers—but not by an increase in accuracy for the differently lying spots either on the trained finger or on the other fingers. An examination of the figures in Table XX shows, however, that the increase in the accuracy of localization in the "ordinary" spots of the untrained fingers does not take place to any appreciable extent in the spots ("1" and "2") which correspond to those which exhibit a marked increase of accuracy of localization in the case of the trained finger; but occurs chiefly in a spot ("3") which on the trained finger exhibits comparatively small increase of accuracy. We are, therefore, probably correct in ascribing the general increase in the accuracy of localization on all the fingers to a general process—perhaps to that associated with "practice."

Another point of interest arises in connection with a possible extension of the effect of the training of the spots on a single finger. In each of the records examined so far, the subject was allowed to know which finger was being stimulated at any one time. Now, for accurate localization of a tactile stimulus, the subject must be aware in the first place of the part of the body which is touched, and in the second place of the place of the spot which is touched upon that part. The part of the body is, of course, a relatively ill-defined concept in the case of most subjects; the subject may have difficulty in defining where the wrist ends and the forearm begins. But, for our purposes, it is perhaps

sufficient to suppose that "front of finger" (or merely "finger") and "place on finger," were two elements in the "position" of the spots which we were examining. Now, error in the first of these elements was eliminated for most of our records by allowing the subject to know which finger was being touched.

But as the experiment proceeded there occurred a definite increase in the accuracy of localization of tactile stimuli on the trained spots of the trained finger. The interesting question arose—does the training of a set of spots on a finger under these conditions enable the subject more accurately to locate tactile stimuli upon that finger than upon the others when he is not allowed to know which finger is being touched? In other words, did the increase of accuracy of localization extend to the element "finger" as well as to the element "place on finger" in the "position" of spots on the trained finger, or was it confined to the element "place on finger"?

To examine this point we used a test in which the "ordinary" spots were touched upon the different fingers in an indifferent order—so that no one finger was often touched twice in succession.

The analysis of such a test is one of difficulty. Here we confine ourselves to the examination of the errors in placing the spot touched irrespective of the fingers, and in localizing the fingers touched irrespective of error in the placing of the spot. Obviously, the finger may be right and the spot on it may be wrongly placed; or the spot may be correctly placed, but upon the wrong finger; or both finger and place on finger may be correctly localized, or both may be wrong. We must refer to a point which touches the accuracy of our results. These tests were comparatively short ones. Except in the case of the last in this series, an average of a little more than 6 stimuli were applied to each finger in each test, and of a little more than 8 to each position of the three spots. In the last test about 50 stimuli were given to each finger, and about 67 to each position of the three spots—that is, about 16·7 stimuli to each individual spot.

We began this test—which may be termed the "unknown finger" test—the day before the training of the "ordinary" spots on the palmar aspect of the right index finger; and continued it, with one exception, every day thereafter. In Tables XXVIII and XXIX the figures are given for the record taken before the commencement of the training of the right index finger and for the two records taken immediately after the commencement of it.

In Table XXVIII the percentage error of localization of each indi-

vidual spot is given without reference to the rightness or wrongness of the finger upon which it was localized. The averages for each of these three spots are rather larger than the corresponding ones for the first five records in this experiment (obtained from Table II). Thus: "1" = 20·5 per cent.; "2" = 30·5 per cent.; "3" = 49·4 per cent.; average of the three = 33·5 per cent. Whereas in the first five records, taken before the training of the right index finger was commenced, these averages were: "1" = 27·3 per cent.; "2" = 41·7 per cent.; "3" = 53·5 per cent.; average of the three = 40·8 per cent.

TABLE XXVIII.—THE PERCENTAGE ERROR OF LOCALIZATION OF THE INDIVIDUAL SPOTS, "1," "2," AND "3," IN THE "UNKNOWN FINGER" TEST UPON THREE SEPARATE DAYS: THE FIRST BEFORE TRAINING OF THE PALMAR SET OF SPOTS ON THE RIGHT INDEX FINGER, THE SECOND ON THE DAY AFTER THE COMMENCEMENT OF THAT TRAINING, THE THIRD ON THE SECOND DAY. IMMEDIATELY UNDERNEATH THESE PERCENTAGES IS GIVEN THE AVERAGE OF THE THREE PERCENTAGE ERRORS; BELOW THAT IS GIVEN THE AVERAGE PERCENTAGE ERROR OF THE BEST FINGER IN THE ORDINARY TEST TAKEN IMMEDIATELY BEFORE THE "UNKNOWN FINGER" TEST; AND BELOW THAT AGAIN IS GIVEN AVERAGE OF THE "AVERAGE ERRORS PER CENT." OF ALL FOUR RIGHT FINGERS (PALMAR ASPECTS) IN THAT ORDINARY TEST.

						DAY OF EXPERIMENT				
						5	6	7	Average	
Spot 1	22·2	..	25·0	..	14·3 = 20·5
Spot 2	42·9	..	15·4	..	33·3 = 30·5
Spot 3	56·6	..	25·0	..	66·7 = 49·4
Average of above errors	40·5	..	21·8	..	38·1 = 33·5
Average error per cent. of best finger	41·4	..	21·1	..	37·2 = 33·2
in ordinary test, same day	(R. 2)	..	(R. 5)	..	(R. 2)
Average of average errors per cent. of	50·9	..	37·3	..	46·8 = 45·0
all four fingers in ordinary test	

A most interesting point is revealed when the average error per cent. of the three spots in each of the "unknown finger" tests is compared with the "average error per cent." of the different fingers in the ordinary test on the same day. It might have been thought that as in this test the spots are touched in an indifferent order upon the different fingers, and that as the accuracy of localization of tactile stimuli differs upon the different fingers when these are examined separately, the error in the "unknown finger" test would be of nearly the same value as that of the average of the errors of the separate fingers in the ordinary test. This is not the case. That average is given for each day on the lowest line of Table XXVIII, and it is seen to be considerably greater than the error in the "unknown finger" test. But the average error per cent. of the best finger (that on which the error was lowest) in the ordinary test approximates very closely to the average error in

the "unknown finger" test. The average error of the best finger is given immediately above that for all the fingers in Table XXVIII. Immediately above it again is given the average error in the "unknown finger" test, and the close approximation is evident. It will be observed that, upon the whole, the average error of the best finger in the ordinary test is somewhat less than the averaged error in the "unknown finger" test.

This result is of course obtained from a relatively small number of observations, and the smallness of these may lead to inaccuracy. But the result is a most curious one. It would seem as if in a manner the "oneness," "twoness," or "threeness" of a spot (that is, its relative position on the finger; the touches, of course, being each single) is a general character common to the spots on the different fingers if no restriction of the touched spots to a single finger is made.

But it must be remembered that in the ordinary test considerable variations occur in the accuracy of the localization of tactile stimuli upon the different fingers. This observation would seem to be antagonistic to that described above. Were the error of localization merely a negative one, and were it due to the elimination of a part of the normal mechanism or to the destruction of a part of the normal process, it would be a matter of difficulty to reconcile the two observations. But perhaps the conception of "positive error" or the distortion of the mechanism (or process) makes such a reconciliation possible.

Thus, if the condition was merely one of negative error the restriction of the test to a single finger would in no manner inconvenience the subject. If he has, as it were, a remnant of the normal process of the cerebrum whereby (on one side) the localization of tactile stimuli is conditioned, the restriction of the investigation to a single finger will in no way impede his correct localizations; while the incorrect ones will be as easily localized upon that finger as upon any other. But if there is "positive error," if the cerebral mechanism is definitely distorted in some manner or other, the subject may feel that a tactile stimulus upon the finger to which the experiment is restricted is really and definitely localized upon another finger—although he knows from the conditions of the experiment that this is not so. Some sort of definite effort is then required on the part of the subject to make the localization on the finger to which the experiment is restricted; and such efforts may well disturb the accuracy of his results. Thus spot "3" on the little finger is touched; the subject may feel that the spot touched is spot "3" on the palmar aspect of the fourth right digit; yet he knows

that it must be located somewhere upon the little finger. He then supposes that the spot is more like spot "2" on the little finger than spot "3" on that finger. The result is that he makes an inaccurate localization—whereas the place of the spot would have been correct if he had made the localization upon the fourth finger—although then the finger element in the localization would have been incorrect.

This supposition is not a fanciful one. The subject of these experiments occasionally told us—in the earlier records—that he felt that the spots which were being touched lay upon another finger than that upon which he knew (from the conditions of the experiment) they must lie. He said, "The other finger seems to draw them away."

The training was not directed to the correction of error as regards the finger upon which the spots lay, but only to the correction of error as regards the place of the spots on the finger. Distortion of the "finger" element in the "positions" of the tactile stimuli may well have been a factor in the error of localization when the test was done on restricted spots on the restricted fingers. When the restriction of the fingers was removed in the "unknown finger" test this distortion may have been removed, and the localization of the place of the spot irrespective of the localization of the finger upon which the spot lay may have been freed.

Another point must, however, be noted in connection with these observations before the training of the ordinary spots on the right index finger. Although the average error of localization of the three spots irrespective of the fingers upon which they lay in the "unknown finger" test was nearly similar to the average error per cent. of the best finger in the ordinary test (in which each finger was examined separately), the incidence of error as between the three individual spots was not similar in the two tests. Thus the localization of spot "1" might be relatively bad in the "unknown finger" test—as compared with that in the ordinary test—and so on, yet the two averages for all three spots might show close agreement.

When the errors of localization of the fingers (irrespective of localization of the spots upon the fingers) are examined it is seen that considerable variation occurs (Table XXIX).

Here the error of hazard should be 75 per cent. The table shows that this is greatly exceeded in the case of the fifth digit—the worst of the four as regards this error; and it is slightly exceeded in the case of the fourth. It was especially in the case of the little finger that the subject in the earlier records felt that the spots touched were on another

finger—usually the fourth. Here is confirmatory evidence of the existence of “positive error” in the localization of tactile stimuli upon a certain finger irrespective of their localization upon that finger itself. As it were, there was a distortion of the element of “finger” in the position of the stimuli applied to a certain set of spots. There was little or no confusion, only a definite reference of the spots to another finger.

TABLE XXIX.—THE PERCENTAGE ERROR OF LOCALIZATION OF THE INDIVIDUAL FINGERS IN THE “UNKNOWN FINGER” TEST ON THE SAME THREE DAYS AS IN TABLE XXVIII.

Finger	DAY OF EXPERIMENT						Average
	5	6	7	8	9	10	
R 2	16.7	83.3	57.1	52.4			
R 3	50.0	28.6	20.0	32.9			
R 4	66.7	83.3	80.0	76.7			
R 5	85.7	100.0	62.5	82.7			

Tables XXX and XXXI compare respectively with Tables XXVIII and XXIX, and they give the corresponding figures for the five days after the training of the palmar set of spots on the right index finger.

TABLE XXX.—THIS TABLE IS SIMILAR TO THAT GIVEN IN XXVIII, BUT THE FIGURES NOW ARE THOSE OBTAINED ON THE FIVE DAYS WHICH IMMEDIATELY FOLLOWED THE TRAINING OF THE RIGHT INDEX FINGER. THE FIGURES IN SQUARE BRACKETS GIVE THE AVERAGES AFTER EXCLUDING RECORD “10.”

DAY OF EXPERIMENT.													
				9		10*		11		12		13	Average
Spot 1	0.0	..	85.7	..	0.0	..	0.0	..	23.7	= 21.9 [5.9]
Spot 2	20.0	..	50.0	..	20.0	..	20.0	..	25.7	= 27.1 [21.4]
Spot 3	37.5	..	75.0	..	0.0	..	12.5	..	50.7	= 35.1 [25.2]
Average of above errors	19.2	..	70.2	..	6.7	..	10.8	..	33.4	= 28.1 [17.5]
Average error per cent. of best finger in ordinary test, same day				16.7	..	6.1	..	15.7	..	7.6	..	23.5	= 13.9 [15.9]
				(R. 2)		(R. 3)		(R. 2)		(R. 2)		(R. 2)	
Average of average errors per cent. of all four fingers in ordinary test				37.6	..	21.3	..	31.9	..	28.3	..	41.9	= 32.2 [34.9]

* On this day the subject had been for too long a walk and had just come in, rather breathless, before the test.

In these tables we are, perhaps, justified in eliminating the record for the tenth day—as on that occasion the subject had just returned from a longer walk than he had yet attempted, and had hurried in the last part of it, as he was late. From Table XXX it will be seen, even including this record, that the error as regards the position of the spots irrespective of the finger upon which they were localized is in every case considerably less than before. As compared with the average of

the percentage errors of localization of each individual spot on all the fingers in the five ordinary tests after the training, the errors for the individual spots in the "unknown finger" test show considerable diminution except in the case of spot "1." Thus: ordinary test (averages obtained from Table XV)—spot "1" = 17.3 per cent.; spot "2" = 35.1 per cent.; spot "3" = 43.3 per cent.; average of the three = 31.9 per cent.; "unknown finger" test—spot "1" = 21.9 per cent.; spot "2" = 27.1 per cent.; spot "3" = 35.1 per cent.; average of the three = 28.1 per cent.

When the averages for the three spots in each record of the "unknown finger" test are compared with the averages for all three spots on each finger and on all the fingers together in the ordinary test (in which the stimuli were restricted at any one time to a single finger) it is again seen that the average in the "unknown finger" test is considerably less than the average for all the fingers in the ordinary test. [Except in the case of record "10," which we may perhaps eliminate.] On the other hand, the average error of localization in the "unknown finger" test is more near to that of the best finger in the ordinary test. Usually it is somewhat greater than the average of the best finger in the ordinary test. Except upon one occasion (record "10"—which we may eliminate) the finger upon which tactile stimuli are most accurately localized is now the trained finger—the palmar aspect of the right index finger.

It would look as if the effect of the training of the right index finger extended to the localization of the spots—irrespective of the finger upon which they are localized—in the unrestricted "unknown finger" test. Table XXXII brings out this point. In that table there is first given the average for each individual spot in the five ordinary test records, and the average of the three averages; alongside these are given the corresponding averages for these spots in the "unknown finger" test—no account being taken of the correctness or incorrectness of the localization of the fingers. The extremely close approximation of the two sets of figures will be observed. On the whole those for the "unknown finger" test are slightly greater—that is, the errors of localization are slightly greater—than for the right index finger in the ordinary test, in which the stimuli were then restricted to that finger. In this case there was at times a fairly close approximation between the individual percentage errors of the three spots on the right index finger in the ordinary tests on the separate days and the errors for three spots (irrespective of finger) in the "unknown finger" tests on the same days.

This was seen, for instance, in record "13," where 200 observations were made, about 67 stimuli being applied to each of the three spots (irrespective of the fingers—i.e., about 17 to each individual spot on each finger. On that day the errors per cent. for the individual spots on the right index finger in the ordinary test were: Spot "1" = 0.0 per cent.; spot "2" = 26.6 per cent.; spot "3" = 43.9 per cent.; average of the three = 23.5 per cent. Whereas the errors in the "unknown finger" test were: Spot "1" = 23.7 per cent.; spot "2" = 25.7 per cent.; spot "3" = 50.7 per cent.; average for the three = 33.4 per cent.

Now the inference from this would seem again to be that the effect of training the "place" element in the localization of tactile stimuli upon the right index finger was extended to the corresponding spots in the unrestricted "unknown finger" tests. Is the "finger" element in that localization also improved by the training?

TABLE XXXI.—THIS TABLE IS SIMILAR TO TABLE XXIX, BUT THE FIGURES NOW ARE THOSE OBTAINED ON THE FIVE DAYS WHICH IMMEDIATELY FOLLOWED THE TRAINING OF THE RIGHT INDEX FINGER.

Finger	DAY OF EXPERIMENT					Average
	9	10	11	12	13	
R 2 ..	42.9 ..	85.7 ..	71.4 ..	80.0 ..	83.7 ..	= 72.7
R 3 ..	40.0 ..	40.0 ..	60.0 ..	33.3 ..	44.4 ..	= 43.5
R 4 ..	80.0 ..	80.0 ..	40.0 ..	57.1 ..	73.5 ..	= 66.1
R 5 ..	50.0 ..	75.0 ..	50.0 ..	71.4 ..	65.4 ..	= 62.4

Apparently not. In Table XXXI the figures for the errors of localization of the different fingers (irrespective of the place of the spots upon them) are given. On comparison with Table XXIX (before training the right index finger, or rather, partly also after the commencement of that training) it will be seen that now the trained right index finger is definitely less accurately localized than before the training. It indeed is now the least accurately localized finger, and the error of localizing it is not markedly less than the error of hazard. The localization of the third digit is also worse than before the training; while the fourth and fifth digits are more accurately localized than before. The figures for record "13" are peculiarly valuable, as they are obtained from a large series of observations—200, about 50 stimuli applied to each finger. The percentage error of the localization of the trained right index finger is here definitely and markedly above the error of hazard. The error of hazard is about 75 per cent.; the error of localizing the right index finger is 83.7 per cent. This points quite distinctly to the presence of "positive error"—to a definite distortion of the "finger"

element in the localization of spots on the right index finger. And this even where the error of localizing these spots on that finger when the experiment is restricted to it has markedly fallen after the training.

TABLE XXXII.—THIS COMPARES THE AVERAGE ERROR PER CENT. OF LOCALIZATION OF TACTILE STIMULI ON EACH INDIVIDUAL SPOT OF THE TRAINED RIGHT INDEX-FINGER IN THE FIVE RECORDS TAKEN AFTER THE TRAINING, ALONG WITH THE AVERAGE OF THE THREE AVERAGES. BESIDE THEM IS PLACED THE AVERAGE ERRORS OF THE THREE SPOTS IN FOUR OF THE FIVE RECORDS OF THE "UNKNOWN FINGER" TEST TAKEN ON THE SAME DAYS (RECORD "10" BEING LEFT OUT). THESE ERRORS ARE IRRESPECTIVE OF THE ERROR OF PLACING THE SPOT UPON THE FINGER IN THIS TEST.

		ORDINARY TEST	"UNKNOWN FINGER" TEST	
		Records 9-13	Records 9, 11, 12, 13	
Spot 1	..	0.00	..	5.9
2	..	20.99	..	21.4
3	..	26.53	..	25.2
Average	..	15.8	..	17.5

There can, we think, be little doubt that in some manner the training of the spots on the palmar aspect of the right index finger has resulted in a general improvement in the localizing of the place of tactile stimuli applied to these spots irrespective of the finger upon which they are localized in the unrestricted "unknown finger" test; but that there is absolutely no improvement in the localizing of tactile stimuli upon the trained finger in that test. As it were, there may well be two elements in the "position" of the stimulus applied to a spot—its location upon a certain and perhaps rather indefinitely bounded portion of the body, and its more exact location within that region. These two elements seem to be independent to this extent, that one may show marked improvement in cases of this sort and after training specially directed to that improvement, while the other may exhibit no such improvement. Where the improvement of one element in "position" occurs it seems to be extended to other similar elements in other similar spots.

(7) *On the Question of the Nature of the (apparent) general Improvement of Localization of Tactile Stimuli which occurred in the untrained Fingers.*

In the preceding subsections of this part of the paper we have noticed that there was an apparent general improvement of localization of tactile stimuli on all the fingers—trained and untrained—in the five

days of the experiment which followed the first period of training. This improvement is seen when we examine the averages for each set of spots, and it might perhaps be inferred that in some way it also was conditioned by the training of the set of spots on the palmar aspect of the right index finger. But we have already pointed out that an examination of the incidences of error for each spot on each finger seems to throw doubt upon the accuracy of such an inference, for the general improvement in the untrained fingers is not conditioned by an increase in the accuracy of localization for the spots which correspond to those which exhibit the greatest improvement upon the trained finger.

Another possibility is that this general improvement on the untrained fingers may be due to practice; while a third (perhaps associated with the second) is that the apparent general improvement is conditioned by the disappearance of the "confusion" error.

In the earlier records of this series the subject repeatedly indicated that he was unable to make a localization, although he was aware that a tactile stimulus had been applied. It happened that, after the period of training of the palmar set of spots on the right index finger, this error practically disappeared from the records. When it occurred we counted it as a wrong localization; but it is clear that, if the subject had made an attempt to localize these stimuli, a certain proportion of them might have been correctly localized. This would have been the case even if the subject had guessed these localizations, for then one-third of them on an average would have fallen upon the correct spot.

But if a certain proportion of a number of answers which in one period of the experiment is counted as definitely wrong, is in a later period of the experiment to be counted as definitely correct, it is clear that an apparent increase in the accuracy of localization may occur. Is the disappearance of the "confusion" error the condition of the apparent general improvement of localization in the untrained fingers?

It is not easy to decide how to treat this phenomenon of the disappearance of confusion. Thus the subject was unable to localize a certain proportion of the stimuli before the period of training. But after that period he was apparently able to localize nearly all the stimuli which were applied to him. We may say that he apparently became able to localize that proportion of stimuli which previously he could not localize.

But *how* did he localize them? There are here many possibilities. Thus he may have localized this proportion of stimuli purely by hazard,

or he may have localized it all on a certain specific spot (that spot being the same one on each finger, or varying on the different fingers); or he may have localized it always on the correct spot (for the "confusion" error occurred when the stimulus was applied to any of the three spots on a finger; or he may have localized it always on incorrect spots; and so on. Finally, he may have localized this proportion of stimuli in the same ratios as between the definitely correctly localized stimuli and the definitely incorrectly localized stimuli at the time when the confusion error was present.

We may, perhaps, regard the "confusion" answer as in some manner conditioned by a stimulus the localization factor of which is subliminal; and the disappearance of the confusion error as conditioned by a fall in the localization threshold. If we accept such a view we would be predisposed to think that the previously "confused" proportion of answers would be localized in the same proportions as those which previously were definitely localized as between right and wrong. The cerebral mechanism is in some manner disturbed by the lesion, and when a stimulus can be localized certain definite errors occur. It would be expected that these same errors would be seen in the proportion of "confused" answers if they became definitely localized ones.

An interesting result is obtained if we analyse the figures for the localizations in each set of spots before and after the period of training, and endeavour to correct for the disappearance of the "confusion" error (Table XXXIII). Thus in the records before the training of the palmar set of spots of the right index finger there was: (1) a certain proportion of indefinite localizations (that is, the "confusion" answers); (2) a certain proportion of definite localizations which were correct, and (3) a certain proportion of definite localizations which were wrong. After the period of training "1" practically disappeared. Now if we take "1" and divide it in the proportions of "2" and "3" (that is, in the ratio of the correct to the incorrect answers) and take that proportion which corresponds to "3" and add it to "3," we obtain a correction of the confusion error and the resultant will be the proportion of definite wrong localizations which would be expected to be made if there was no "confusion." This has been done in Table XXXIII, and it will be seen that the computed figure for definite incorrect localization agrees very closely with the actual figure for incorrect localizations obtained in the records after the period of training and when the "confusion" answer had disappeared. But it does so

only in the case of the untrained fingers. The actual figure in the case of the trained right index finger is very much smaller than the computed.

TABLE XXXIII.—TABLE SHOWING THE POSSIBLE EFFECT OF DISAPPEARANCE OF THE "CONFUSION" ERROR. EXCEPT THOSE IN COLUMN "G," THE FIGURES REFER TO THE EXPERIMENTS BEFORE THE TRAINING OF THE RIGHT INDEX FINGER. THEY ARE GIVEN FOR EACH ASPECT OF EACH FINGER, AND FOR THE THREE INDIVIDUAL SPOTS OF THE PALMAR SET ON THE RIGHT INDEX FINGER. COLUMN "A" GIVES THE PERCENTAGE OF CORRECT LOCALIZATIONS; COLUMN "B," THE PERCENTAGE OF "CONFUSION" ANSWERS; COLUMN "C," THE PERCENTAGE OF DEFINITELY WRONG LOCALIZATIONS; COLUMN "D" GIVES THE PERCENTAGE OF DEFINITE LOCALIZATIONS (RIGHT AND WRONG); COLUMN "E" GIVES THE PERCENTAGE OF "CONFUSED" ANSWERS WHICH WOULD HAVE BEEN EXPECTED TO BE WRONG IF THE PROPORTION OF ANSWERS IN COLUMN "B" HAD BEEN DIVIDED AS BETWEEN DEFINITELY RIGHT AND DEFINITELY WRONG IN THE SAME PROPORTIONS AS THOSE IN COLUMNS "A" AND "C"; IN COLUMN "F" THE FIGURES ARE OBTAINED BY ADDING THOSE IN COLUMNS "C" AND "E" TOGETHER—THUS GIVING THE TOTAL PERCENTAGE OF DEFINITELY INCORRECT LOCALIZATIONS IF THE "CONFUSION" ANSWERS WERE ELIMINATED; AND IN COLUMN "G" THE ACTUAL FIGURE FOR PERCENTAGE ERROR OBTAINED AFTER THE TRAINING OF THE RIGHT INDEX FINGER (WHEN "CONFUSION" DISAPPEARED) IS GIVEN FOR COMPARISON.

Finger		A	B	C	D	E	F	G
Palmar	R 2	57.30	14.37	28.33	85.63	4.75	33.08	15.72
	R 3	68.02	7.37	24.61	92.63	1.96	26.57	29.68
	R 4	53.28	10.20	36.52	89.80	4.15	40.67	43.06
	R 5	56.94	7.61	35.45	92.39	2.92	33.37	40.68
Dorsal	R 2	71.44	11.79	16.77	88.21	2.24	19.01	21.62
	R 3	81.24	5.50	13.26	94.50	0.77	14.03	15.72
	R 4	73.20	9.18	17.62	90.82	1.78	19.40	20.62
	R 5	67.38	12.49	20.13	87.51	2.86	22.99	22.16
R 2 Spot	"1"	67.57	8.11	24.33	91.90	2.14	26.47	0.00
	"2"	37.50	25.00	37.50	75.00	12.50	50.00	20.98
	"3"	65.00	10.00	25.00	90.00	2.78	27.78	26.53

This would seem to show that the apparent general improvement of localization of tactile stimuli in the case of the untrained fingers is actually referable to the disappearance of confusion—which synchronized with the period of training; but at the same time it shows definitely that the improvement of localization in the case of the trained finger is not referable to this, and it strongly emphasizes our suggestion that this was indeed conditioned by the training.

The same table gives information with regard to the three individual spots on the palmar aspect of the right index finger. Of these, spots "1" and "2" showed a very definite improvement in localization, while spot "3" showed a much smaller improvement. When the "confusion" error before the training is corrected in the manner described above, it is found that in the cases of spots "1" and "2" the computed

figure is very much greater than the figure for the definite incorrect answers after the period of training. But the computed figure for spot "3" is only slightly less than the actual one. This seems to show that the effect of the training was to increase the accuracy of localizing stimuli which were applied to spots "1" and "2," but not to increase it for stimuli applied to spot "3"—or to increase it very slightly for that spot.

If we assume that the proportion of previously "confused" answers was definitely localized by hazard after the disappearance of the confusion—instead of being definitely localized in the same ratio as the definitely localized answers (correct and incorrect)—there is again a fairly close correspondence between the computed figures and the actual figures for definitely localized answers after the disappearance of the "confusion" phenomenon. These figures are given for the percentages of definitely localized incorrect answers in Table XXXIV—where they are compared with the figures computed in the manner described before. In each case the difference between the computed and the actual figure is given.

TABLE XXXIV.—IN THIS TABLE COLUMNS "F" AND "G" ARE THE SAME AS THE CORRESPONDINGLY MARKED COLUMNS IN TABLE XXXIII. COLUMN "H" GIVES THE DIFFERENCE BETWEEN THE TWO, "+" SIGNIFYING THAT THE REAL FIGURE (I.E., THAT IN COLUMN "G") IS GREATER THAN THE COMPUTED. IN COLUMN "I" THE FIGURE IS COMPUTED ON THE ASSUMPTION THAT THE PREVIOUSLY "CONFUSED" PROPORTION OF ANSWERS WAS LOCALIZED BY HAZARD AFTER THE DISAPPEARANCE OF THE CONFUSION—THAT IS, THAT TWO-THIRDS OF THIS PROPORTION OF THE ANSWERS WAS INCORRECT. COLUMN "K" IS A REPETITION OF COLUMN "G"; AND COLUMN "L" GIVES THE DIFFERENCE BETWEEN THE NUMBERS IN COLUMNS "I" AND "K."

Finger	F	G	H	I	K	L
Palmar R 2 ..	33·08	15·72	-17·36	37·91	15·72	-22·19
R 3 ..	26·57	29·68	+ 3·11	29·52	29·68	+ 0·16
R 4 ..	40·67	43·06	+ 2·39	43·32	43·06	- 0·26
R 5 ..	38·37	40·68	+ 2·31	40·52	40·68	+ 0·16
Dorsal R 2 ..	19·01	21·62	+ 2·61	24·63	21·62	- 3·01
R 3 ..	14·03	15·72	+ 1·69	16·92	15·72	- 1·20
R 4 ..	19·40	20·62	+ 1·22	23·74	20·62	- 3·12
R 5 ..	22·99	22·16	- 0·83	28·46	22·16	- 6·30
R. 2, Spot "1" ..	26·47	0·00	-26·47	29·47	0·00	-29·47
"2" ..	50·00	20·98	-29·02	54·17	20·98	-33·19
"3" ..	27·78	26·53	- 1·25	31·67	26·53	- 5·14

It will be seen that the computed figure is still larger than the actual one in the case of the trained finger; as well as in the case of the two individual spots which showed the greatest improvement in that finger. In the case of the percentage errors of localization for the palmar aspects of the untrained fingers a very exact correspondence

between the computed and the actual figures occurs. But there is a less close correspondence when the figures for the dorsal aspects of the fingers are examined. There in every case the computed figure is greater than the actual one.

It would, therefore, appear that the improvement in accuracy of localization of stimuli applied to the trained palmar set of spots (or to two of these three spots when the figures are analysed more closely) cannot be ascribed to the disappearance of the "confusion" error which synchronized with the period of training. The apparent slight general improvement in localization seen in the palmar sets of spots of the three untrained fingers may be explained as due to the disappearance of the confusion error, whichever of the two manners of correcting for that error we use; but, if it be corrected for on the assumption that the previously unlocalized proportion of answers becomes localized in the same ratios (as between definitely right and definitely wrong) that obtain in the previously definitely localized answers, it would appear that instead of an apparent slight general improvement of accuracy of localization after the training there is a slight actual deterioration. In the case of the dorsal sets of spots, if the correction is made as above there would also appear to be a slight actual deterioration; but if the correction is made on the assumption that the previously unlocalized proportion of answers was localized by hazard, there would appear to be a greater actual improvement of accuracy of localization.

There is less variation in the results if the correction is made in the first manner than if it is made in the second, and we think that we are probably justified in the assumption that, at this stage in the experiment, the general improvement in accuracy of localization of the untrained sets of spots was an apparent one only, and conditioned by the disappearance of the "confusion" error.

VI.—CLINICAL DESCRIPTION OF THE CASE.

Family history.—J. H. L., the patient, is the eldest son in a family of three. He was born in 1886. Both parents are alive and healthy. There is no history of nervous disorder in the family.

Previous history.—The patient left school at the age of twelve, having reached Standard IV. For some years he worked on a farm with his father who was a brewer's maltster. At the age of 23 he joined the Army, and served from March, 1909, to March, 1912. On leaving the Army he worked as a platelayer on the railway.

On the outbreak of war he was called up, and went abroad with the 1st British Expeditionary Force.

With the exception of influenza in 1910 he had no illness of any description.

History of present illness.—The patient was wounded near Ypres on October 26, 1914, about 2.30 p.m. His company was in the trenches repelling a German attack. He was in a leaning attitude firing as rapidly as he could. While in the act of pressing the trigger he felt a sudden shock in his head, and lost consciousness for about five minutes. When he recovered he found himself in a sitting posture. He could feel blood running over his face. He was blind and unable to understand what his comrades were saying. At the moment when he was knocked out he had been speaking, and he now found himself unable to utter any word except "Yes."

When the Royal Army Medical Corps orderlies gave him a drink of water he was given much more than he required, as he kept on repeating "Yes," "Yes." He had a vague idea that he was being captured by Germans and started to struggle. He found, however, that he was quite unable to use either limb on the right side.

He lay in the trench until nightfall and was then removed on a stretcher to the Medical Officer's dressing station. He was very weak from loss of blood.

He was conveyed by motor ambulance to Boulogne and on reaching hospital was taken straight to the operating theatre. On waking next morning he felt very weak and unable to move. His speech had not returned, but he could now understand what people were saying and could see.

During the first day in hospital he had a vivid dream of walking under the Eiffel Tower.

His speech and ability to read remained in abeyance for about a week, but long before he could speak he was able to sing songs which he knew by heart.

During the first few days of his illness he had incontinence of faeces, but no difficulty with regard to micturition. On the fourteenth day after admission the right side of his face twitched for a few seconds. One day he saw a magazine lying on the bed next to his own and for some hours he lay trying to puzzle out the title on the front page. Suddenly it came back to him, and he alarmed the ward by exclaiming "Bystander" in a loud voice. After this his vocabulary rapidly grew, but he stammered a great deal when speaking. All parts of speech came back with equal rapidity.

On December 15, 1914, he was shipped to Southampton and sent to a hospital in Wandsworth. At this time he was still paralysed on the right side. At the end of a month he was allowed to get up. He felt very weak and with assistance could only walk a few yards.

During his residence in this hospital he suffered considerably from his eyes. He had much photophobia, and felt dizzy when he looked at objects. For a fortnight he wore an eyeshade.

With regard to his paralysed limbs, recovery of power began in the lower extremity, and was much more rapid than in the upper limb. The right side of his face was also paralysed, and at first his tongue used to fall to one side, so that he bit it during sleep.

For many weeks he was quite unaware of the position of his affected limbs in bed, and had to grope for his right hand. Five weeks after admission to hospital in London he had a "seizure" affecting the right side. He had been gargling his throat with salt and water, and swallowed some the "wrong way." While in the act of coughing violently the muscles on the right side of his body began to twitch, producing irregular movements of the right upper and lower limbs. Consciousness was preserved, and in about five minutes the attack passed off.

This epileptiform seizure was followed by a change in his mental state. On the following day he developed the delusion that other patients were making disparaging remarks about him. He had several more seizures before leaving this hospital, and found that their duration was shortened if he remained quite motionless and silent.

While in bed his right lower extremity was habitually flexed at the knee. He made an effort to straighten it one day by pressing his foot against the bed-rail. He became suddenly giddy and appears to have lost consciousness, and to have remained in a stuporose state for several days. Recovery was followed by the appearance of fresh delusions. A magazine illustration of famous generals which he saw in the hospital library suggested to him that he must be Napoleon's grandson. This delusion was accompanied by auditory hallucinations. A voice repeatedly told him of his imperial rank.

His explanation of this delusion is worth recording. The date of publication of the magazine was that of his father's birthday. This occurred to him when he was looking at the photograph of the Kaiser and Napoleon, and it at once became clear to him that he must be Napoleon's grandson.

On March 1, 1915, he was transferred to the Royal Victoria Hospital, Netley. He had so far recovered that he was able to walk to the station. His memory for this period is good. He remembers giving particulars of himself and being put to bed. He became excited and repeatedly shouted "Three cheers for the Red, White and Blue." Every time he said this a "voice" echoed his words. At the end of three days he was transferred to the Military Hospital, Maghull. At the station he struggled and was put in the guard's van. He was seized with the idea that he was being electrocuted through the floor, as he had a sensation of pins and needles in his right lower limb, and involuntary movements on the same side. This delusion persisted for some weeks. Not only did he hear imaginary "voices" talking about electrocution, but a patient in the bed next his own talked a great deal about electricity. In this way he was encouraged in his false belief.

When examined on the day after admission he was found to be dull and lethargic. He expressed delusions of grandeur, and exhibited "negativism." He had difficulty in selecting words. Articulation was slow and slurring. Paresis of both extremities on the right side was noted. He showed coarse tremor, slight nystagmus, and increased deep reflexes. Ankle-clonus existed on the right side.

During the summer of 1915 his mental state underwent but little change.

His delusions persisted, and he was inclined to be aggressive. Motor power gradually returned in his affected limbs. He continued to have fits, and on three occasions lost consciousness; usually the fits were Jacksonian in type, and presented the following characteristics. A sudden sensation of vibration or electricity in the right arm, accompanied by a feeling of faintness, warned the patient to lie down. He remained conscious, could see and hear everything, but was unable to speak. Twitching of his muscles next occurred; the thumb was always first affected; then, in order, the hand, elbow, shoulder and body on the affected side. The leg was affected last, while the face always escaped. On several occasions the head was deflected to the right. Each fit was followed by transient motor weakness in the affected limbs, while articulation became more impaired for several days.

In the later months of 1915 his attacks became less frequent and his mental state improved greatly; he became tractable and lost his delusions. Auditory hallucinations persisted until the month of November.

The following notes on his condition were made during the last week of November, 1915.

Clinical examination.—The patient is a tall, well-developed man; he is right-handed. His pulse is irregular and intermittent. His urine contains no albumen and his radial arteries are not thickened. The wounds of entry and exit, which mark the course of the bullet which penetrated the patient's skull, lie in the following situations: The former lies 12 cm. posterior to the nasion and 5 cm. to the left of a line joining that point with theinion; the latter (wound of exit) measured along this sagittal line lies 29 cm. posterior to theinion, and 3 cm. to the left of the median plane. The area of each of these cranial wounds is equal to that of a sixpenny-piece. Immediately anterior to the wound of exit there is a large trephine opening in the parietal bone, in which pulsations can be observed. It has an antero-posterior length of 11 cm., and a breadth of 4 cm. Its anterior extremity lies 22 cm. posterior to theinion and 3 cm. to the left of the median plane. Pressure on the edges of this foramen causes intense local pain. He is observant and intelligent.

We take the opportunity of remarking here how much we are indebted to the patient himself for our subsequent experiments, which would hardly have been possible without his intelligent co-operation and patience. His memory and attention are good. He has no disturbance of perception. Articulation is slow and slightly impaired; he stumbles and hesitates when pronouncing certain words. He is able to read, and writes with his left hand. In carrying out simple orders he confuses the right side with the left. For example, when told to close his right eye he almost invariably closes his left. Occasionally he uses wrong words, and has difficulty in finding the word he wants. In the addition of figures he frequently makes mistakes. There is no apraxia. He states that when excited he becomes deaf in the left ear.

Special senses.—Smell, taste, and hearing are normal. The visual fields are restricted, especially that of the left eye.

Cranial nerves.—The pupils are equal and react normally to light and on

accommodation. Ophthalmoscopic examination reveals evidence of previous retinal change. The disc margins are slightly obscured and the vessels near the disc ill-defined. There is very slight motor weakness of the right side of the face; the right eye is habitually more open than the left. When he closes the right eye there is overaction of the facial muscles on the same side. The corneal reflexes are equal. The functions of other cranial nerves are normal.

Motor system.—The left limbs are unaffected. The size of the muscles is equal in the two upper limbs, but their tone is much increased on the right side. There is slight contracture of the fingers. The range of movement is normal at the right shoulder, elbow and wrist joints, but movements of the thumb and individual fingers are much restricted. The right upper limb is much weaker than the left; the grasp of the right hand, measured with the dynamometer, is only 23 kgm., while on the normal side it is 45 kgm. Voluntary power is especially weak in the interossei and in the intrinsic muscles of the thumb. Movements of extension of the digits are much weaker than those of flexion. Adduction of the thumb is very imperfectly performed, and a movement of flexion of the thumb accompanies flexion of any of the fingers. The thumb is usually flexed at the metacarpophalangeal joint, adducted, and extended at the interphalangeal joint. Loss of voluntary movement is more complete in the fifth digit than in the index finger. Full extension or flexion of the little finger is impossible, and the attempt is accompanied by movements of other fingers. Owing partly to this motor weakness and partly to the co-existent ataxia, the limb is only used for general movements at the large joints, and is useless for finer actions. The patient holds his pipe, writes, dresses himself, &c., with the left limb.

The right upper limb is often colder than the left and slightly cyanosed.

Abrupt irregular involuntary movements may frequently be observed in the thumb and fingers. These take the form of a sudden flexion at the basal joints of one or more fingers, or an isolated movement of the thumb. They are sometimes entirely absent for several days, and are most noticeable before seizures.

The patient is unaware of their occurrence unless his attention is specially directed to his affected limb. The patient has himself observed that these involuntary movements can be increased by making strong volitional movements of the normal limbs or of the right foot; he has further observed that he can restrain them by concentrating his attention on his hand. Thus, for example, strong voluntary movements of the toes of either foot may produce involuntary movements of the affected fingers, and if, while continuing these voluntary movements, the patient directs his attention to his hand, he may succeed in arresting or diminishing the involuntary movements of the fingers. The act of yawning is accompanied by flexion of the thumb and fingers and of the wrist of the right upper limb. All movements of the right upper extremity are very ataxic. When the patient extends both upper limbs horizontally in front of him, the right arm performs swaying movements as soon as the eyes are closed.

There is no wasting of the right lower limb; the tone of its muscles is increased. There are no contractures and the range of movement is unrestricted. There is slight motor weakness in the affected limb. There are no involuntary movements. Marked ataxia exists and is well seen when the patient performs the heel to knee test.

Gait: In walking the right upper arm is adducted and remains rigidly applied to the side; movement takes place at the elbow, the forearm swinging loosely. The right lower limb executes a slight movement of circumduction at the hip. In descending or ascending stairs it is raised higher than necessary, and is then planted in an uncertain manner. The right shoulder droops perceptibly.

Reflexes.—The right arm-jerks are exaggerated; the knee- and ankle-jerks are exaggerated. Those on the right side are brisker than on the left. Ankle-clonus cannot be obtained. The plantar reflex is usually absent on the right side, on the left a normal flexor response is obtained. After a Jacksonian fit, however, an extensor response exists for some hours on the right side. The abdominal reflexes are equal on the two sides.

Subjective sensations.—He has frequent headaches on the left side of the head, and local pain in the neighbourhood of the cranial wound. In his right upper limb he has often a feeling of numbness, and sometimes there is a feeling as though the whole of the right side did not exist. The knowledge of position of his right upper limb is very imperfect when he is without the guidance of vision.

Tactile sensibility.—He cannot appreciate cotton wool touches with certainty on the tips of the fingers of the right hand, nor on their dorsal surfaces. On these areas his answers are irregular, and he often entirely fails to appreciate the stimulus. Elsewhere on the right upper limb cotton wool touches are recognized, but there is a subjective difference; the feeling is "weaker" on the right side and "not so tickly" as on the normal side. The same difference is felt on the right malar region, and on the right ear there is a "vast difference." On the right side of the abdomen and on the right lower extremity, a wisp of cotton wool rubbed across the skin seems less distinct than on the left side. He is unable to define exactly this feeling, and states that on hair-clad parts the cotton wool produces a "creeping sensation," which is diffuse, being felt over a wide area of the leg. For the purpose of examining with graduated tactile stimuli, hairs mounted on matches were roughly calibrated by measuring on a balance (in grains)¹ the force exerted by them in bending. A series of nine hairs exerting pressures varying from $\frac{1}{2}$ to 140 gr. was obtained. The method of applying the graduated tactile stimuli was that adopted by Head and Holmes. A hair is selected producing a stimulus just above the minimum threshold to which the normal hand reacts with constancy when the stimulus is applied sixteen times in the minute; the same hair is used in the same manner to a corresponding part of the affected hand, and then more powerful hairs are used, up to those exerting many times the pressure.

¹ Metric system weights were unobtainable in this hospital.

The strength of the stimulus is then decreased to the hair with which the testing was begun, ending up with a series of contacts on the normal hand.

The following result was obtained when hairs of various bending strains were applied sixteen times in the minute to an area of skin on the dorsal aspect of the hands (between the third and fourth metacarpal bones).

A stroke represents a correct answer; a nought, that the patient did not respond; a broken stroke represents an hallucination.

Hairs (bending strain in grains)	Normal hand (left)	Affected hand (right)
7	1111111111111111	—
7	—	0110000000100000
12	—	0001011111110111
20	—	1111111111111010
30	—	111111110111011
40	—	111111110011011
80	—	1111011111111111
40	—	0111111010111100
30	—	111111011111100
20	—	000111100100011
12	—	0000100111010010
7	—	0100001010000000
7	1111111111111111	—

Thus it is apparent that on the normal hand a perfect series of answers can be obtained with a hair of 7 gr. bending strain, but on the affected hand the answers are slower (the patient remarking, "It don't send the message to the brain quite so soon") and inconstant. There is a persistence of sensation, and hallucinations occur. No definite threshold is obtained. On the flexor surface of the right forearm the answers are still irregular, and are much disturbed by hallucinations and persistence of sensation. On the upper arm (bicapital area) evidence of a definite threshold is obtained, and there are no hallucinations. On the face a threshold can be obtained with hair "3." The record is not disturbed by hallucinations, and there is no slowness in response. The sensation evoked by the hair is not quite similar on the two sides. On the sole of the foot it is possible to obtain evidence of a definite threshold; hallucinations, however, are numerous. On the dorsal surface of the foot, on the inner aspect of the leg, and on the right side of the abdomen (umbilical level) the answers continue to be slow, irregular, and disturbed by hallucinations.

The following record illustrates the condition.

ABDOMEN (UMBILICAL LEVEL).		
Hairs	Normal side (left)	Affected side (right)
3	1111111111111111	—
3	—	1111111111111111
8	—	1111011111111111
30	—	1111111111111111
40	—	1111111101111111
70	—	1111011111111111
90	—	1111111111101111
70	—	1111111111110001
40	—	1101110011111111
30	—	1101111101111111
8	—	1110010100101111
3	—	1001110110010100
3	1111111111111111	—

Pressure touch.—Tested roughly with the pulp of the observer's finger or by a blunt-pointed rod (whose movement through a cylinder is resisted by a rubber band), showed an uncertainty of response, and a tendency to evoke hallucinations on the right hand and forearm. Pressure touch on the right side of the body does not always evoke the same sensation as on the left. Thus, pressure with the blunt end of a pencil on the right cheek, or on the right side of the abdomen, evokes a sensation as though a much broader object were being applied. There is a feeling of "spread-outness" which is not experienced on the normal side.

Roughness.—The same thresholds are obtained on both sides with Graham Brown's aesthesiometer. With sand-paper, four grades of roughness can be readily identified. The relative roughness of any two grades can also be distinguished. No difference can be detected between the two sides.

Tickling and scraping.—No difference to tickling or scraping can be detected between the palms or the soles of the feet.

Sensibility to pain. (a) *Superficial pain.*—When tested with a needle on the right cheek and on the right forearm, the patient states that the prick is less sharp than on the normal side, but the pain evoked is as great. On the right upper arm there is slight hyperæsthesia to pinprick. On other areas no difference can be detected.

(b) *Pressure pain.*—No difference between the two sides can be obtained. Measured prick was not employed.

Vibration.—On the right side the vibrations of a heavy tuning-fork (C) evoke sensations which are "not so plain" as on the normal side. The vibrations are appreciated for a shorter period on the right upper limb than on the left. Thus, when the patient can no longer appreciate the vibration on the right radial styloid process, it can be recognized for a period of seventeen seconds on the corresponding point on the left side. After the tuning-fork can no longer be appreciated on the left styloid process it is recognizable on the right side for a period of twelve seconds. There is thus a difference of five seconds between the two sides, and on the back of the hand it is much greater. No difference between the two sides can be obtained on the upper arm or on the lower limb.

Temperature.—The paretic limb is frequently colder than the left, but when this condition is not noticeable, definite changes in the response to thermal stimuli can be demonstrated. Thus, on the normal left palm the neutral zone lies between 27° C. and 31° C. On the right palm all temperatures between 26° C. and 37° C. appear to be neither hot nor cold. The power of comparing thermal stimuli is also defective. On the right side temperatures of 41° C. and 47° C. are correctly appreciated as hot, but he is quite unable to say which is the hotter. Similarly, he cannot discriminate between water at 15° C. and water at 20° C., whereas on the normal side he can always tell which of the two is the colder. Further, his answers on the right side are slow and irregular. On the sole of the right foot the neutral zone lies between 23° C. and 25° C.; on the normal foot it lies between 28° C. and 30° C. Here

again, however, his ability to discriminate the relative warmth of two tubes is diminished.

The application of a heat stimulus sometimes evokes a burning or slightly painful sensation on the right foot, when on the left side it is quite comfortable. On the same area a cold stimulus is described as feeling "all over the place," whereas on the normal side it is localized to one area. He has noticed while washing that water which is only sufficiently hot to be quite comfortable on the normal hand may cause a "stinging pain" on the right hand, which persists for several minutes after withdrawal.

Sense of position. (a) *Recognition of posture.*—The patient's recognition of the posture of his right upper limb is grossly defective. If the defect is measured by the method introduced by Horsley, and modified by Head and Holmes, the records obtained when the affected hand seeks the normal forefinger are very much better than when the patient attempts to point to the affected forefinger with his normal hand.

The examination of separate segments of the limb (by asking the patient to imitate, as exactly as possible with his normal limb, the posture of the affected part) shows that a grave loss is present, which is most profound in the distal segments of the limb. When one of the fingers or the thumb is placed in a particular attitude while the patient's attention is diverted, he is quite unable a moment later to imitate successfully the posture with his normal digits.

With regard to movements of the hand, at the wrist-joint he is less inaccurate, but confuses an attitude of flexion with one of extension. He does not imitate with the normal forearm attitudes of supination and pronation. The upper arm also shares in the defect, but in a much less marked degree. Recognition of posture is also impaired in the lower limb.

(b) *Recognition of passive movement.*—The appreciation of passive movements is very much impaired. Movements are appreciated long before their direction can be recognized. Indeed, he is quite unable to recognize the direction of movement in the thumb or in any finger, unless hyperextension or very full flexion is carried out. All the digits can be moved through a wide angle before the movement is perceived. At the wrist extreme flexion or extension only can be recognized, and movements through a very wide angle cannot be appreciated. Recognition of the direction of the movements of pronation and supination is grossly defective.

At the elbow-joint the direction of movement is usually correctly appreciated, when the angle of movement exceeds 60° .

At the shoulder-joint these defects are much less obvious. The recognition of passive movement and the direction of movement is also very defective in the toes and ankle. The occurrence of numerous hallucinations of movement can be noted at all limb joints, except those of the shoulder and elbow.

Localization, as tested by the modified Henri method, is found to be much affected on the right hand and forearm; and, to a lesser degree, on the right upper arm, right side of the face, and right lower extremity. Occasionally (on the right side) the patient states that he has no knowledge of the locality

of the contact, but in the majority of instances he localizes the stimulus in some false direction. This holds good, not only for the proximal segments of the limb, but also for the right fingers and palm.

For testing the patient's power of recognizing the position of a spot stimulated the pressure-touch instrument was used, the touches being repeated until the patient could appreciate the contact.

The following record was obtained by making the contacts in an irregular order on the dorsal aspect of each digit:—

Digit	Correct	Localized proximal	Distal	Localized on wrong digit	"Don't know"
Normal hand (left)					
Thumb ..	10	0	0	0	0
Index finger ..	10	0	0	0	0
Middle „ ..	7	1	1	1	0
Ring „ ..	8	1	1	0	0
Little „ ..	7	1	2	0	0
Abnormal hand (right)	Correct (or on same level)	Proximal	Distal	Wrong digit	"Don't know"
Thumb ..	1	2	1	6	0
Index finger ..	2	2	0	6	0
Middle „ ..	2	3	0	5	0
Ring „ ..	2	1	0	7	0
Little „ ..	2	0	1	7	0

Thus on the normal (left) digits he correctly localizes 42 contacts out of 50; while on the abnormal (left) digits only 9 are correctly placed. On another occasion, out of 20 painful stimuli equally distributed on the terminal phalanges of the right digits only one was correctly localized, 5 were incorrectly localized on the base of the thumb, and in three cases the patient had no idea of the situation of the stimulus. The dorsum of the hand was selected for a comparison of the accuracy of localization of tactile stimuli with accuracy of localization of painful stimuli; 35 touch stimuli and (afterwards) 35 pain stimuli (pin prick) were given; 7 stimuli in each case being applied to the area of skin above each metacarpal bone. The stimuli were applied in an irregular order and the patient attempted to localize them in the usual manner upon the hand of a model.

In the following table the distances of the points wrongly indicated from the spots touched or pricked are recorded in centimetres (to the nearest whole centimetre)—“C” indicating that the stimulus is correctly localized:—

		<i>Tactile stimuli (dorsum of right hand).</i>										(stimuli)
Skin areas over		i	ii	iii	iv	v	vi	vii				
1st metacarpal	..	10	.. 8	.. 4	.. 8	.. 6	.. 10	.. 8				
2nd	..	6	.. 6	.. 3	.. 2	.. 5	.. C	.. 2				
3rd	..	C	.. 5	.. 4	.. 2	.. 5	.. 3	.. 5				
4th	..	1	.. 1	.. 1	.. 4	.. C	.. 5	.. 2				
5th	..	4	.. C	.. C	.. 1	.. 4	.. 2	.. 2				
		<i>Painful stimuli (dorsum of right hand).</i>										(stimuli)
1st	..	1	.. 3	.. 2	.. 2	.. 1	.. 6	.. 1				
2nd	..	2	.. 2	.. 1	.. 2	.. 2	.. 2	.. C				
3rd	..	2	.. 2	.. C	.. 6	.. C	.. 2	.. C				
4th	..	2	.. 1	.. 1	.. C	.. 1	.. C	.. 1				
5th	..	1	.. 3	.. 2	.. 3	.. C	.. 3	.. 2				

On the normal (left) hand in only one instance did the error in localization exceed 2 cm.

It would appear from the above observations that erroneous localization is present, both where the stimulus is one of pressure-touch and where it is a prick, but that in the latter case the error is not so great as in the former.

On the terminal phalanges this difference is less obvious. Out of 50 touch stimuli 12 are correctly placed, while out of a similar number of prick stimuli 17 are correctly localized (in 11 instances he had no idea of the locality of the stimulus). The patient remarked, "A prick seems often to concentrate at the wrist."

On the right forearm the power of localization is plainly defective, but the defect is not so great as in the case of the hand of fingers. Out of 20 pressure-touch stimuli 10 are localized in false positions which vary from 5 to 14 cm. in distance from the spot touched. In no instance does the patient fail to make a localization.

On the right upper arm localization is also disturbed, but is more accurate than on the right forearm.

Comparison of the accuracy of localization on the two sides of the face demonstrates a slight disturbance of localization on the right cheek.

The power of recognizing the position of stimulated spots on the right foot is much impaired. Out of 50 tactile stimuli applied either to the great toe or to the little toe, the number of errors on the left side is 7 and on the right side 26. The defect is present, although in a lesser degree, in the case of the right leg.

Compass test.—The power of discriminating the two points of the compasses is gravely affected on the right upper limb.

On the palm the patient cannot recognize the "two-ness" of two points synchronously applied, even when the distance between them is 6 cm.; whereas, on the normal left palm, no error occurs when the points are 1.5 cm. apart.

On the right side no threshold can be obtained for the fingers, palm, nor for the dorsal surface of the hand; nor can a threshold be obtained for the right forearm (neither surface), right upper arm, right side of the face, right forehead. Neither can a true threshold be found for the right lower extremity, nor for the right side of the abdomen. The power to recognize the double nature of the compass points is also lost on the right hand, when the points are applied successively.

The following are some of the records obtained:—

Normal (Left)		Abnormal (Right)	
Palm	..1.5 cm.	{ 1: 11 111 1 11 11 2: 111 1 1 11 11 1	1.5 cm. { 1: 11 1111X 11X1 2: X1X 1XX XX X1
			4 cm. { 1: X XX 1XX 1X 1 1 2: 1 1 111 11 1 1X
			6 cm. { 1: 1 11 111 111 X 2: X1XX 11X 1 1X

	Normal (Left)	Abnormal (Right)
Forearm (flexor surface) 5 cm.	$\left\{ \begin{array}{l} 1: 111 \ 11 \ 1 \ 111 \ 1 \\ 2: \ 11 \ 1111 \ 111 \ 1 \end{array} \right.$	5 cm. $\left\{ \begin{array}{l} 1: 11 \ 1 \ 111 \ 1111 \\ 2: X \ X \ XX \ XXX \ XXX \end{array} \right.$
Upper arm .. 6 cm.	$\left\{ \begin{array}{l} 1: 1 \ 111 \ 1 \ 111 \ 1 \ 1 \\ 2: 11 \ 1 \ 1 \ 11 \ 111 \ 1 \end{array} \right.$	15 cm. $\left\{ \begin{array}{l} 1: \ 1 \ 1X \ XXX \ X \ XX1 \\ 2: XIX \ 1X \ 11 \ 11 \ 1 \end{array} \right.$ 6 cm. $\left\{ \begin{array}{l} 1: 11 \ 111 \ X \ 10 \ 11 \\ 2: X \ 11 \ 111 \ XXX \ X \end{array} \right.$
Face (cheek) .. 2.5 cm.	$\left\{ \begin{array}{l} 1: 111 \ 11 \ 1 \ 11 \ 11 \\ 2: \ 1 \ 111 \ 11 \ 11 \ 11 \end{array} \right.$	10 cm. $\left\{ \begin{array}{l} 1: 111 \ 1 \ X1X \ 1 \ X1 \\ 2: 11X \ X11 \ 11 \ 11 \end{array} \right.$ 3 cm. $\left\{ \begin{array}{l} 1: X11 \ X \ X \ XX \ X \ 1 \ 1 \\ 2: 1X1 \ 1 \ 1 \ 1X \ 1X \ 1 \end{array} \right.$
Sole of foot .. 2.5 cm.	$\left\{ \begin{array}{l} 1: 1 \ 1 \ 111 \ 111 \ 11 \\ 2: 11 \ 11 \ 111 \ 1 \ 11 \end{array} \right.$	6 cm. $\left\{ \begin{array}{l} 1: 11 \ 11X \ 11 \ 11 \ 1 \\ 2: 11 \ 11 \ XX1 \ 11 \ 1 \end{array} \right.$ 4 cm. $\left\{ \begin{array}{l} 1: X \ 1X \ XX \ 1XX \ X \ 1 \\ 2: 1 \ 11X \ XX \ 1 \ X1 \ X \end{array} \right.$
Dorsum of foot 4 cm.	$\left\{ \begin{array}{l} 1: 11 \ 1 \ 11 \ 111 \ 11 \\ 2: 11 \ 111 \ 111 \ 1 \ 1 \end{array} \right.$	10 cm. $\left\{ \begin{array}{l} 1: 1 \ 11 \ 11X \ 11 \ 11 \\ 2: XIX \ 11 \ 1X \ X \ 1 \ 1 \end{array} \right.$ 5 cm. $\left\{ \begin{array}{l} 1: XX \ 1 \ 1X1 \ XXX \ 1 \\ 2: X111 \ 1 \ 1 \ XX \ 11 \end{array} \right.$
Leg (inner aspect) 6 cm.	$\left\{ \begin{array}{l} 1: 1 \ 111 \ 11 \ 11 \ 11 \\ 2: 11 \ 1 \ 11 \ 111 \ 1 \ 1 \end{array} \right.$	10 cm. $\left\{ \begin{array}{l} 1: 1 \ 11X \ 1X \ 1X1 \ 1 \\ 2: 111 \ 11 \ 1 \ 11 \ XX \end{array} \right.$ 8 cm. $\left\{ \begin{array}{l} 1: 1 \ 11 \ 111 \ 1 \ 11 \ 1 \\ 2: XX1 \ X \ XX \ X \ X \ XX \end{array} \right.$
Pectoral region (3rd rib) 7 cm.	$\left\{ \begin{array}{l} 1: 1 \ 11 \ 111 \ 1 \ 11 \ 1 \\ 2: 1 \ 11 \ 111 \ 11 \ 1 \ 1 \end{array} \right.$	15 cm. $\left\{ \begin{array}{l} 1: 111 \ X \ 1 \ 111 \ 11 \\ 2: 1 \ X1 \ 11 \ XX \ X \ XX \end{array} \right.$ 7 cm. $\left\{ \begin{array}{l} 1: 111 \ 11 \ 1 \ X \ 11X \\ 2: 1 \ 11X \ X1 \ 11 \ 11 \end{array} \right.$
		15 cm. $\left\{ \begin{array}{l} 1: X \ 1XX \ 11 \ 1 \ 111 \\ 2: 111 \ 1 \ 1 \ 11 \ 11 \ 1 \end{array} \right.$

His replies are characterized by slowness, uncertainty, and irregularity. On some occasions, when twoness is recognized, he states that the points feel very close together—although actually they may be separated from one another by as much as 5 cm.

Power of recognizing weight.—On the normal hand his power of appreciating weight is quite acute, but on the right hand it is much impaired. With the hand completely supported he can easily distinguish, on the left (normal) side, between 4 oz. and 8 oz., and 16 oz. and 24 oz., but on the abnormal right hand he cannot.

The power of recognizing addition and subtraction of weight is also much impaired.

With unsupported hands, when a weight is placed in each hand and the patient is asked to "weigh" them by raising and lowering his hands, the errors are equally gross. He thus cannot distinguish with certainty between 1 lb. and 1½ lb.; nor between 1 lb. and 2 lb.

Appreciation of size.—The patient has completely lost the ability to recognize differences in size of objects placed upon his right palm, nor can he distinguish between the head and the point of a pin when they are gently applied to the skin.

Appreciation of two-dimensional shape.—He is equally at fault when asked to recognize various shapes when they are placed in contact with the surface of the right palm; on the left normal palm he has no difficulty in distinguishing them.

Appreciation of three-dimensional form.—The patient is quite unable to recognize common objects placed in his right hand when his eyes are closed. These objects are at once recognized when placed in the left hand. Thus :—

Object	Reply—right hand	Reply—left hand
1. An ink-pot	"Something hard, solid and cold."	"An ink-pot" (immediately).
2. A large tuning-fork ..	"Something hard, light and cold."	"A tuning-fork."
3. A rolled-up handkerchief ..	"Something soft and tepid." ..	"A handkerchief."
4. Small nail-scissors ..	"Cannot describe it." ..	"Nail-scissors."
5. A penny	"Just a feeling in my hand."	"A penny."
6. A large pocket-knife ..	"Hard, that's all I can say." ..	"A knife."

Appreciation of texture.—In spite of his power of recognizing roughness or smoothness, he has great difficulty in appreciating texture with the right hand. The following record illustrates his condition :—

Material	Reply—right hand	Reply—left hand
1. Velvet	"Soft, like rubber." ..	"Velvet."
2. Silk	"Coarse calico." ..	"Silk."
3. Towel	"Ribbed surface" ..	"Coarse towelling."
4. Flannelette ..	"Like calico." ..	"Flannelette."
5. Satin	"Not quite satin." ..	"Satin."
6. Velvet (again) ..	"Piece of coarse substance." ..	"Velvet."

With his right hand he is quite unable to appreciate any difference between velvet and flannelette; with his left hand he can distinguish them without difficulty.

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RECORDS OF SPEECH IN DISSEMINATED SCLEROSIS.

BY E. W. SCRIPTURE, M.D., PH.D.

§ 1.—METHOD OF RECORDING AND ANALYSIS.

SPEECH in disseminated sclerosis has been described in so many conflicting and indefinite ways that an attempt at accurate fixation by graphic records and analyses of the curves seems desirable.

The speech is recorded by the phonautograph method. The patient speaks into the mouthpiece of a wide rubber tube (fig. 1). This leads to a metal tube covered by a flexible membrane (fig. 2). The movements of the membrane are recorded by a lever writing on a moving blackened cylinder.

A record of "ah" sung by a normal voice is reproduced in fig. 3. The waves begin faintly; they rise quickly to full intensity. They are quite regular. In the record of a vowel each wave represents one vibration of the glottis. The length of a wave records the duration of a vibration. Slow vibrations, which produce low tones, are recorded as long waves; fast vibrations, or high tones, as short waves. Since the speed of the recording drum is known, a measurement of the length of a wave will give the duration of the vibration and the pitch of the tone. For example, with a surface speed of 1 mm. equal to 0.0085 sec., a wave of 0.9 mm. is the record of a vibration whose duration was $0.0085 \times 0.9 = 0.00765$ sec. If one vibration occupied this time, then the frequency, or the number of vibrations per second, would be $1 \div 0.00765 = 131$.

Measurement of the first six waves in fig. 3 gives the following results:—

Wave length	0.9 mm.	..0.9 mm.	..0.9½ mm.	..0.9½ mm.	..1.0 mm.	..1.0½ mm.
Duration	..0.00765 sec.	..0.00765 sec.	..0.00808 sec.	..0.00808 sec.	..0.00850 sec.	..0.00893 sec.
Frequency	... 131 vib.	.. 131 vib.	.. 124 vib.	.. 124 vib.	.. 118 vib.	.. 118 vib.

On cross-section paper the curve is supposed to be laid along the X-axis and a dot to be placed above each wave at a height proportionate to the frequency. Such a "melody plot" for the entire record of fig. 3 is shown in fig. 4. A line drawn smoothly through these dots shows



FIG. 1.—Recording speech by the phonautograph method. The vibrations and puffs of air pass to a flexible membrane, whose movements are recorded on a revolving drum by means of a light lever.



FIG. 2.—Speech recorder. The wide metal tube is covered with oiled silk, whose movements are amplified by a light lever. This recorder is a development of the Scott phonautograph by the Abbé Rousselot.

how the voice rises and falls. If the larynx could produce a tone of absolutely constant pitch, the melody plot would be a straight horizontal line. Actually the melody plot, even in song, is a perfectly straight line only for short distances.

A record of "I'd like to go home" by a normal voice is given in fig. 5. It begins with the vibrations of the larynx during "I." These gradually increase in intensity. They are suddenly cut short by the descent of the line which records the movement of the tongue in closing the mouth to make the "d." The line at the base level records the sound while the tongue was held firmly across the mouth-passage—the "occlusion" of the "d." It has faint waves; these

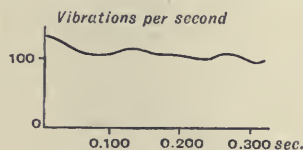


FIG. 4.—Melody plot to fig. 3. The length of each wave in fig. 3 is measured. The duration and frequency are calculated. The record in fig. 3 is supposed to be laid along the X-axis. A dot is placed above each wave on the scale of frequency. The series of dots is the "melody plot." A line drawn through them shows that the voice fell rapidly for the first few vibrations and then fluctuated with a slow fall just above 100 vibrations per second.

show that the larynx vibrated during the "d." The stronger waves that follow belong to "l" and later to "i." They are cut short by a fall not quite so sudden as for "d"; this is produced by closing the back of the tongue against the hard palate and velum to produce the "k." The straight line is ended by a sudden rise. We know that the latter portion of the straight line represents the occlusion of "t" and the sudden rise its "explosion," because in the spoken words the "k" sound is immediately followed by "t" without any break. There are no vibrations at this place, therefore the larynx was silent during "k" and "t." After the rather breathy explosion of "t" there follow a few waves that register the very short indefinite vowel "o" of "to." The line for "g" is like that for "d." The long series of large waves

Fig. 3.—Record of "ah" sung by a normal voice. Each wave registers one vibration of the larynx. The waves begin smoothly and evenly. The height rapidly increases during the first ten waves. The waves are apparently of nearly even height and length throughout. The slight general rise and fall of the record indicates some variations in breath pressure.

registers the sounds between "g" and "m." These include the two vowels "o" and the "h" between them. In normal speech the larynx usually continues to vibrate during an "h" between two vowels. The "m" is recorded by a base line with faint waves ending in a kind of explosion.

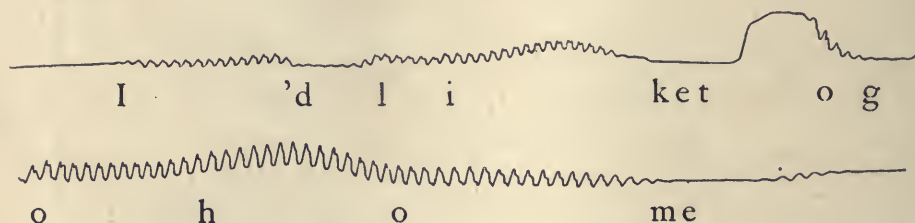


FIG. 5.—Record of "I'd like to go home," by a normal voice. The vibrations of the vowel "I" are cut short by a fall of the line at the beginning of "d." Faint vibrations are seen during the "d." The larger vibrations for "l" are followed by still larger ones for "i." These are cut short as the line descends for "k." The straight line for "k" is continued for "t"; there is no division between them. There is a strong upward movement that registers the puff of air (explosion) at the end of "t." The vowel "o" is very short. The "g" has faint waves. From the beginning of "o" through "h" and the next "o" there is an unbroken series of strong vibrations; the "h" between the two vowels is itself made into a vowel. The faint vibrations of "m" end in stronger ones.

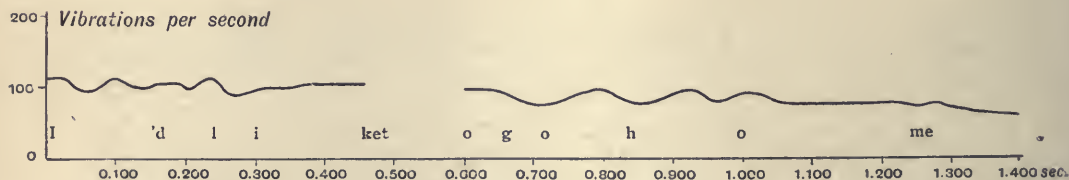


FIG. 6.—Melody plot to fig. 5. The speech curve in fig. 5 is supposed to be laid along the horizontal axis. The whole phrase lasted 1,400 seconds. Above the point where each wave of the record would come, a dot is placed that indicates on the vertical scale the number of vibrations per second that would be made by a tone with this wave length. The series of dots is the "melody plot." A line drawn through these dots indicates the rise and fall of the voice. The melody is seen to be constantly rising and falling in smooth fluctuations: this is a fundamental characteristic of a normal voice. For "kt" there are no dots, because the larynx does not vibrate during those sounds. The phrase starts at a tone of about 120 vibrations a second and falls slowly to one of about 60 at the end; the fall of an octave is the most frequent one in declarative sentences spoken by a Londoner.

The melody plot for fig. 5 is given in fig. 6. The dots lie somewhat irregularly around a line that is drawn to indicate their general position. These irregularities indicate on a magnified scale the normal minor irregularities of the laryngeal vibrations. The general course of the laryngeal tone is indicated by the line itself. We notice that the vowel starts at a little above 100 vibrations per second in "I." It fluctuates up and down within moderate limits during the sounds that follow. At "k" it suddenly stops, because the larynx does not vibrate during

this sound and the following "t." For the remainder of the sentence it continues the tone at about 100 vibrations for an instant and then gradually falls with small fluctuations to the end. These small fluctuations are essential characteristics of normal speech.

§ 2.—RECORDS OF CASES WITH NO PERCEPTIBLE SPEECH ABNORMALITY; DEMONSTRATION OF LARYNGEAL ATAXIA.

The patient, E. B. E. (National Hospital), female, aged 32, stated that at 21 years of age she had felt numbness in the right leg. At the age of 28 she lost entirely the use of the right arm and leg. This was attributed to "neurasthenia" by the family physician. She became apparently well in about a year and did not notice anything troublesome. Two months ago she had noticed that the right leg was shaky and that her gait was unsteady. On examination the knee-jerks were found to be greatly increased on the right and slightly on the left. There was some uncertainty of the right hand only. Some nystagmus was present. Nothing abnormal could be detected in the voice. She herself had never noticed anything abnormal, although she sang considerably.

Records of this well-established case with no perceptible voice signs showed that the consonants were all correctly formed, and that there were no changes in intensity, duration, melody or rhythm. The vowel curves, however, revealed a peculiar abnormality. Instead of the even series of waves as in fig 3, the record of a vowel by this patient invariably showed the presence of peculiar irregular waves such as may be seen in the piece of vowel reproduced in fig. 7.



FIG. 7.—Beginning of "ah" sung by E. B. E. The waves at the start show peculiar vibrations.

The patient, E. C. (National Hospital), aged 47, had had diphtheria at 17 years of age. At 20 she suddenly lost the sight of the right eye for a time. At 27 she lost the use of the left hand temporarily; the right leg became troublesome some time later. At 37 there was entire loss of speech for a fortnight. At 45 there was difficulty in micturition. Lately the left leg was painful and the walk bad. She had had no speech trouble since the temporary one referred to above. She says she has had trouble in singing hymns ever since the attack of diphtheria. Examination showed: nystagmus and pale discs; intention tremor most marked in right extremities; very bad walk; no abdominal reflexes; exaggerated knee-jerks and ankle-clonus: extensor plantar reflex on right; diminished sensitiveness of right leg. No defects of speech could be observed by the ear except that she seemed to become tired when speaking.

A piece from a record of "ah" spoken by this patient is reproduced in fig. 8. At the start it shows the same peculiar vibrations as those seen in fig. 7. There were no other abnormalities in the speech record.

The patient, H. H. (National Hospital), had been wounded in the left hip, left arm and left shoulder during the Boer War in 1901. After being in the hospital for two months, he was invalided home. On coming out of the hospital he noticed a slight lameness in the right ankle. This became gradually worse. He became lame in both legs and seemed to "walk from the hips" (1911). Under treatment in 1912 he began to improve gradually. Some years ago he had had double vision but had recovered perfectly after three months. His arms had never been affected. There had never been any trouble in speech. On examination his walk was poor and he looked tired. The knee-jerks were both exaggerated; there was ankle-clonus on both sides. Otherwise there was nothing abnormal. His speech, in particular, seemed perfectly normal.

FIG. 8.—Beginning of "ah" spoken by E. C. The peculiar vibrations are seen at the start.

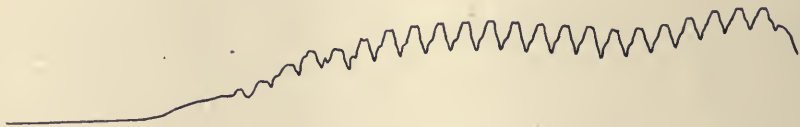


FIG. 9.—Beginning of "I'd like to go home," by H. H. After several peculiar vibrations the waves of the initial vowel become regular.

At one place only in the records does anything abnormal appear. The beginning of one registration of "I'd like to go home" is reproduced in fig. 9. The peculiar vibration is evident.

Before going further it will be well to consider the meaning of the peculiar vibrations referred to.

In the first place they have been found in the records of every case of disseminated sclerosis so far recorded (twenty in all), regardless of whether any speech defect could be detected by the ear or not. If this continues to happen as the number of cases increases, we approach nearer and nearer to a firm belief that disseminated sclerosis always reveals itself in these peculiar vibrations.

Each wave in the record is a registration of a vibration in the tone from the larynx. If the larynx could produce a tone of perfectly constant pitch, all the recorded waves would be of the same length.

When a rising or a falling tone is recorded, the waves change gradually in length, from short to long and from long to short. The peculiar vibrations do not show rising or falling tones, but are the records of very brief imperfections.

The differences and changes in pitch of the laryngeal tone are produced by altering the tension of the vocal cords. Shortening waves indicate increase of tension, lengthening waves indicate decrease of tension. The peculiar waves noticed in all the records are registrations, not of ordinary changes of tension, but of jerky irregularities of tension of the vocal cords.

The vibrating body in the larynx that produces the tone consists of the vocal muscles (usually called the vocal cords) and the thyreo-arytenoid muscles (formerly called the external thyreo-arytenoid). These are stretched by the action of the crico-thyroid muscles. The tension—and consequently the pitch of the tone—is controlled by the interaction of these muscles. Normally the action is smooth and the waves of the vowels are regular as in fig. 3. Even the most rapid shake of the voice that can be produced voluntarily is registered as a series of even waves in which the eye cannot detect any variations. When the waves of such a tremor are measured under the microscope, the change in pitch is found to be even and never jerky. Indeed it is quite incredible that any voluntary movement can be so suddenly jerky as those recorded for disseminated sclerosis. The time occupied by the crico-thyroid jerk in these records is often less than 0.005 sec. The fastest time yet recorded for tapping with the finger is 0.07 sec., and for a voluntary shake of the crico-thyroid is 0.16 sec.

The involuntary shaking or quavering of the voice in emotions is not more rapid than that which can be produced voluntarily; it never consists of brief jerks. Records of real tremor of the voice such as occur in neurasthenia, senility, paralysis agitans, &c., differ from voluntary tremor only in the period of oscillations in pitch. They never show the peculiar vibrations. Both shaking and tremor of the voice consist of oscillations in pitch, not of brief jerks.

Peculiar irregular vibrations in the vowels have been found in the records of diseased conditions of two kinds. In the one class the vocal cords flap loosely instead of vibrating firmly. I have found such waves in the records of progressive bulbar paralysis, and of a normal voice with rattling crico-arytenoid joints, &c. In all these cases the irregular waves were more or less irregular throughout or for long stretches of the vowel. There was never a brief jerk at the beginning

or the end of a vowel. The other class includes the spastic conditions. Records of spastic speech occasionally show irregularities in the wave lengths at the beginning of vowels.

The discharge from a motor nucleus depends on the condition of the nucleus itself. Irregularity in the discharge indicates a defect of control. It is well established that for all muscular movements there is a system of control, termed "taxia," which co-ordinates them so that the resulting motion is properly and smoothly carried out. A defect of the control is called "ataxia." Here we have a defect in the control of the crico-thyroid muscle in tensing the vocal cords. The peculiar vibrations are thus records of laryngeal ataxia.

The peculiar vibrations were found in these cases nearly always at the beginning or the end of a vowel, rarely during the main part of the vowel. When the adjustment of tension has been once attained, the patient seems to have little difficulty in keeping it; the ataxia appears when he tries to attain an adjustment or to let go of it. This also explains why the voice defect is unperceived in such cases, except perhaps as involving some fatigue. With more marked cases the peculiar vibrations appear at various other points.

If laryngeal ataxia is thus established as a sign of disseminated sclerosis that can be registered at a period when no speech trouble can be detected by the ear, we can hope to detect the disease at the earliest possible moment.

§ 3.—RECORDS OF CASES WITH VARIOUS ABNORMALITIES; INTENTION TREMOR; BREATHING ATAXIA; STACCATO SPEECH; ELISION AND ATTRACTION; ANATAXIA; DURATION OF SOUNDS; SCANNING SPEECH.

Some of the further peculiarities of speech in this disease will now be studied.

J. H. (National Hospital), tramway motorman, aged 42, fell four years ago when his tram was struck. He was reported as suffering from contusion and shock. Being unable to go back to work he was examined by a neurologist. He admitted that he had noticed a difficulty in walking and speaking before the accident, but claimed that the trouble had greatly increased since then. Examination showed a well marked case of disseminated sclerosis with particular affection of the speech organs and the left leg. His claim against the tramway company for compensation was partially admitted. His speech appeared very laboured and tight. The larynx could be seen to move up and down irregularly in the neck. In a throat examination the glottis could be seen to open and shut irregularly while "ah" was sung.

When first interviewed, J. H. seemed to have some of the excessive contraction of the lips and tongue that is usual in stutterers. This disappeared shortly as he became at ease, and no expression could be obtained in the records. He admits some trouble in speech in childhood, and the nature of his speech when excited shows him to have been a stutterer.

Fig. 10 is from a record of "ah" sung by J. H. The beginning of the record shows the peculiar vibrations in a most marked manner; they occurred constantly in his records. The figure also shows that the vowel waves swell and fade away in alternations of intensity. The melody plot is given in fig. 11. During

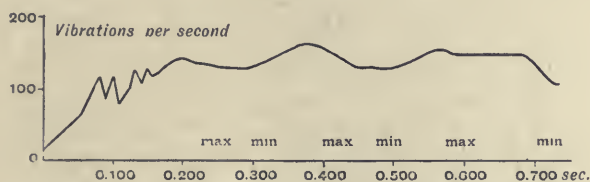


FIG. 11.—Melody plot to fig. 10. Violent jerks appear at the start. The pitch of the tone varies considerably. There is no definite relation of the pitch to the maxima and minima of intensity.

the louder portions the vowel waves themselves were shorter and during the weaker portions longer. There were thus two factors in the irregularities, namely, intensity and pitch.

Repeated irregularities of this kind bear some resemblance to a tremor. Since they occur only when voluntary action is attempted, they have been termed "intention tremor." "Intention tremor" is, however, merely ataxia plus the effort to control it.

The patient, G. C. (National Hospital), at age 22 noticed a weakness in his right instep after walking; two years later the foot dragged. At age 25 he found that he was not able to talk fluently; his words seemed to get tied up with his tongue and he often could not get them out unless he paused; his lips seemed in his way (as if he had "too much lip") and his whole mouth seemed not properly constructed. Somewhat later tremor appeared in his

FIG. 10.—Beginning of "ah" sung by J. H. The record begins with peculiar vibrations. The waves soon become apparently regular in length. Their height increases and diminishes as in a tremolo; this is due to ataxia of breath control.

Fig. 12.—Beginning of “ah” sung by G. C. The peculiar vibrations at the start are very marked.

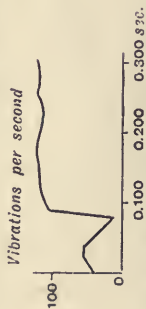


Fig. 13.—Melody plot to fig. 12. After the violent initial jerks the tone becomes quite steady.

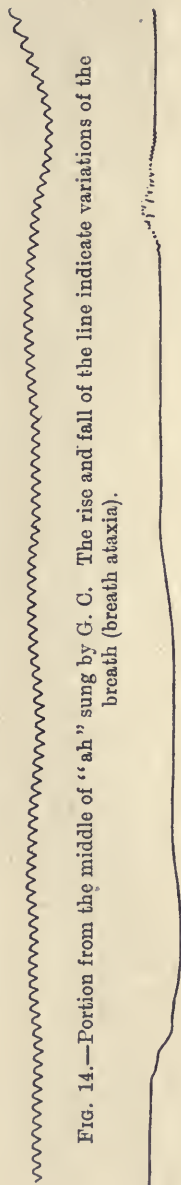


Fig. 14.—Portion from the middle of “ah” sung by G. C. The rise and fall of the line indicate variations of the breath (breath ataxia).



Fig. 15.—Portion of a record of “ah” sung by J. E. Instead of an even series of waves as in fig. 3 the vowel waves appear in pieces that rise and fall quickly like the explosion of “t” in fig. 5. The vowel was in fact composed of a series of pieces shot out separately with silences between them.

hand; his vision was often blurred and double. For the last two years the symptoms have been increasing and extending. Now at age 29 his voice sounds monotonous with laboured enunciation. He often inserts "er" and often lets off some breath at the end of a phrase. On examination his face looked very tired; his walk was irregular; nystagmus was present. The abdominal reflexes were lacking; the knee-jerks were exaggerated and equal; there was no ankle clonus; the plantar reflexes were extensor. In making records he would often halt for a very brief instant before a consonant. Difficult combinations of consonants, like "Peter Piper's peppers," troubled him considerably, but he always practised them, so that unless they were new to him he could speak them fluently.

The peculiar vibrations in G. C.'s records are exemplified by those in fig. 12 for the beginning of "ah" sung. The melody plot is given in fig. 13.

The ataxia in breathing is well shown by the rise and fall of the line in a record of "ah" sung by G. C., reproduced in fig. 14.

At age 14, J. E. (National Hospital), noticed that people sometimes could not understand what he said. Two years later he noticed a difficulty in walking. In the fourth year of his disease he began to shake; in the fifth he was obliged to give up work.

At the age of 24, my observations (by ear) of his speech were summarized as follows: Speed slow, about one-third normal; force increased; vowels normal in length or nearly so; consonants greatly lengthened, three to twelve times; spaces of silence inserted after many consonants and vowels; gasps occasionally inserted; explosions of consonants increased; vowels often brought out as a series of two or more explosions preceded and followed by silence.

In the attempt to sing "ah" the patient emitted a series of explosions with silences between them. A portion of such a record is given in fig. 15. The portions of straight line represent absolute silence and holding of the breath. The sudden and extreme risings in the line register the explosions between silences. The fine waves register the vibrations of the larynx.

Observation of the patient during such an attempt to sing "ah" showed that the muscles of the mouth were held rigid. The abdomen was held in violent contraction without tremor. To resist the resulting pressure either the diaphragm or the glottal lips must have been strongly contracted. As this contraction was relaxed momentarily, the breath burst forth. In addition to all this, the muscles of face, arms and legs were strongly contracted. The violence of the



FIG. 16.—Record of "Peter" by J. E. The "P" has a proper explosion (raised line) followed by a few vowel vibrations. It is followed by a long line indicating absolute silence. The vowel "e" is shot out in two pieces. For the "t" there is a wavering outgo and intake of breath followed by an explosion. A silence occurs before the vowel "er" is shot out.

contractions was indicated by the perspiration that was produced and the fatigue of which he complained.

In a word like "Peter" (fig. 16) he closes his lips for the "p" and opens them for its explosion, as shown by the straight line with the rise at the end. The following straight line indicates silence and shows that everything is cramped tight. The vowel "e" is emitted in two explosions followed by a silent cramp. The peculiar rise and fall of the line for "t" shows that instead of the normal silence (occlusion) air was emitted and drawn in; this was due to a coarse jerk of the tongue whereby it could not keep its position firmly across the mouth passage.

Observation of the abdomen during the word "baby" showed that it gave three strong movements. One of these occurred with the explosion of each "b." The third was violent and prolonged after the final vowel. It was evidently produced to cut off the vowel to a normal length; there must have been joint contraction of the diaphragm and abdominal muscles whereby further expulsion of breath was hindered. The patient said he felt he must make this cramp after each word as otherwise he does not feel that the word is finished. He can postpone this final cramp for several seconds, but he does not feel comfortable until he makes it. Instead of ending a word by relaxation as we normally do, he—in order to avoid continued vowel explosions—ends it by a cramp. The action finally becomes a habit.

Silent spaces (cramps) were habitually inserted by him after both vowels and consonants. Including the silent spaces and the explosions, the vowels were much lengthened, the consonants often immensely so. Inspiratory gasps were frequent.

The speech of this patient brings out forcibly two factors that characterize the speech of this disease, namely, ataxia and the effort to control ataxia. For the latter process a special term is needed; "anataxia" conforms to the habits of medical terminology. The speech of this disease, like the stamping gait of tabes, is an expression of ataxia plus anataxia, and not of ataxia alone.

The speech records do not yet afford any direct conclusion whether the ataxia is motor or sensory. The fact that tabetic patients with sensory ataxia complain of loss of sensation as the cause of their irregular movements, while sclerotic patients never do so, seems to justify the general conclusion that the ataxia in disseminated sclerosis is motor.

The speech of this patient also affords a good illustration of the overaction of hypertonic muscles.

The history of P. G. (National Hospital), aged 16, taken in October, 1911, states that about a year previously he had been troubled by mistiness before the eyes, squint and double vision. About eight months later there was unsteadiness of the legs and arms; he walked badly and could not hold a cup. After about eleven months he had been troubled by precipitate micturition. He was described as being very intelligent and having a good memory. All his eye movements were jerky and inco-ordinated; the left external rectus was almost totally lacking in power: there was nystagmus in all directions. His speech was described as slow and stumbling. There was inco-ordination in arms and legs. There was a slight tremor on both sides; this was increased in movement. The gait was unsteady; the Romberg sign was absent. In February, 1914, he had had an "attack" while at work in which he "contorted," lost consciousness and was very sick. At home he had seven or eight fits more, in which he lost consciousness; the convulsions occurred on the right side, involving face, arm and leg. On admission to the National Hospital in March, 1914, he is described as good-natured, stupid, with poor attention and memory. His optic discs were highly coloured; there was a rhythmic moving of the pupils during convergence; there was ample nystagmus of moderate speed. He was affected by double vision. There was weakness in the region of the left facial nerve. His speech was described as dysarthric; the right arm was spastic; both legs were spastic, the right more so. Only feeble movements were possible; there was no incontinence of urine.

Records of P. G.'s speech were made in April, 1914. Upon being told to sing "ah" it was a long time before he started. A breathy, wavering "ah" was produced. With each repetition he made the sound successively shorter, probably from fatigue. Although he was able to make all sounds correctly, he frequently slurred them or left them out in actual speech, thus he said "go' morning" and "hippopot'mus." In repeating the phrase "Peter Piper's peppers" he regularly took a breath before and expelled it after each word, thus:—

↗ Peter↘ ↗ Piper's↘ ↗ peppers↘

An example of elision was seen in—

↗ Peter↘ ↗ Piper↘ ↗ peppers↘

and of attraction in—

↗ Peter's↘ ↗ Piper's↘ ↗ peppers↘

The "s" was often enormously prolonged, as "s-s-s-s-stead, yes-s-s-s, pleas-s-s-s-sure."

The peculiar laryngeal vibrations were constantly present in his records.

These phenomena can be reduced to ataxia and spasticity with the efforts to control them. The initial hesitation is merely to get the muscles under control. The wavering is due to a breath ataxia. The

fatigue is naturally due to the great muscular effort. The slurring and elision result from the excessive efforts at control. The shouting out of a series of words in separate breaths indicates inability to control the breath ataxia for any considerable time. The prolongation of the "s" was presumably due to difficulty in releasing an excessive contraction of the tongue. The peculiar laryngeal vibrations are the direct registration of laryngeal ataxia as explained above.

The shooting out of each word by a separate breath impulse is probably what has given rise to the description "staccato speech." This staccato is evidently the result of an attempt to control the breath ataxia. Although such staccato effects are found in some cases, they are absent in most. Staccato speech indicates disseminated sclerosis—unless further research finds it in other diseases—but it is quite wrong to say that the speech of this disease is characteristically staccato.

One special fact requires explanation, namely, the attraction of "s" in "Peter's Piper's peppers." In general paralysis the cases of attraction, elision, transposition, &c., are attributed to a cortical defect that produces a symptom-group known as "apraxia." I have observed precisely similar cases in epilepsy, paralysis agitans and mental backwardness, where the cause was certainly not the cortical lesion that produces apraxia, but was simply mental dulness or sluggishness. It is impossible to decide at present whether these cases in disseminated sclerosis indicate apraxia or mental degeneration.

The patient, E. A. E., was admitted to the London County Council Asylum at Claybury at the age of 19 on a certificate which stated that "she is continually crying and singing; she imagines she is in a caravan and sees imaginary horses in the ward." On admission her sensations were described as normal, as were also the pupillary reflexes. She was not able to make many movements owing to the loss of power and tone of the whole of the muscles of the body. These were somewhat wasted all over, and no particular group of muscles seemed to have been picked out. Her legs were useless. She could hardly raise or move them in bed. There was marked tremor of the right arm and less of the left. The tremor increased on attempting to drink a glass of water. There was a constant coarse tremor of the head. There was no reflex on stimulation of the sole of the foot. There was increase in the reflex jerks of the muscles of arm and hand, on the left perhaps more markedly than on the right. There was nystagmus on looking every way except downward. She said she was unable to swallow as well as she used to. She was unable to get rid of bronchial secretion easily. Her eyesight was failing. Her memory was fair. Her speech was laboured. She was suffering from mental confusion and was anxious, depressed, and emotional. There was some history of her having been in a hospital for a similar difficulty a year or more ago.

She seemed to be an advanced case of this disease, showing the somewhat unusual features of very rapid progress and great mental disturbance. When I attempted to take records the patient simply asked continually, "Have I a father and mother?" With some difficulty she was induced to speak into the apparatus. After a time she became quite at ease.

She died twelve days after admission. At the autopsy, the following observations were made: There was wasting of the leg muscles, especially on the right. There was no thickening or opacity of the cerebral membranes. Extensive sclerotic areas could be seen in various parts at the base of the brain. The lungs showed areas of broncho-pneumonia.

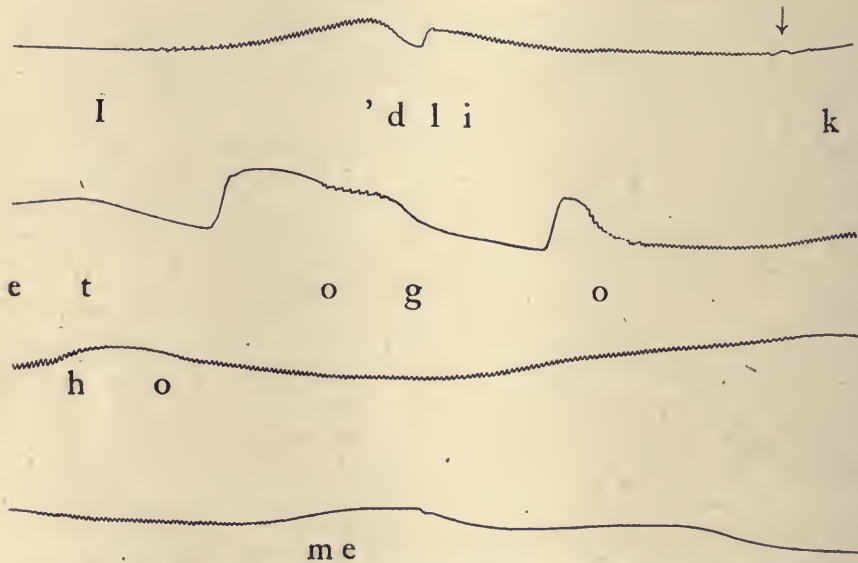


FIG. 17.—Record of "I'd like to go home," by E. A. E. The record is nearly twice as long as a normal one. The "d," "t," and "g," all show their occlusions (descent to the base line) with explosions (sharp rise). The "k" shows a rising line that indicates an incomplete closure of the mouth by the tongue. The vowels are very long. The "m" is lost in a long expulsion of breath.

A record of "I'd like to go home," by E. A. E., is shown in fig. 17. The "I" is breathy (as shown by the rise of the line) and long. The "d" is not a sudden drop in the line as it should be normally, but is a gradual descent; this denotes that the first portion is breathy. The explosion is even more distinct than in a normal record. The "l" is quite distinctly marked. The "i" is long. The slow descent of the line shows that the "k" is fricative instead of occlusive, that is, that the tongue does not completely close the mouth passage. The "k" is quite

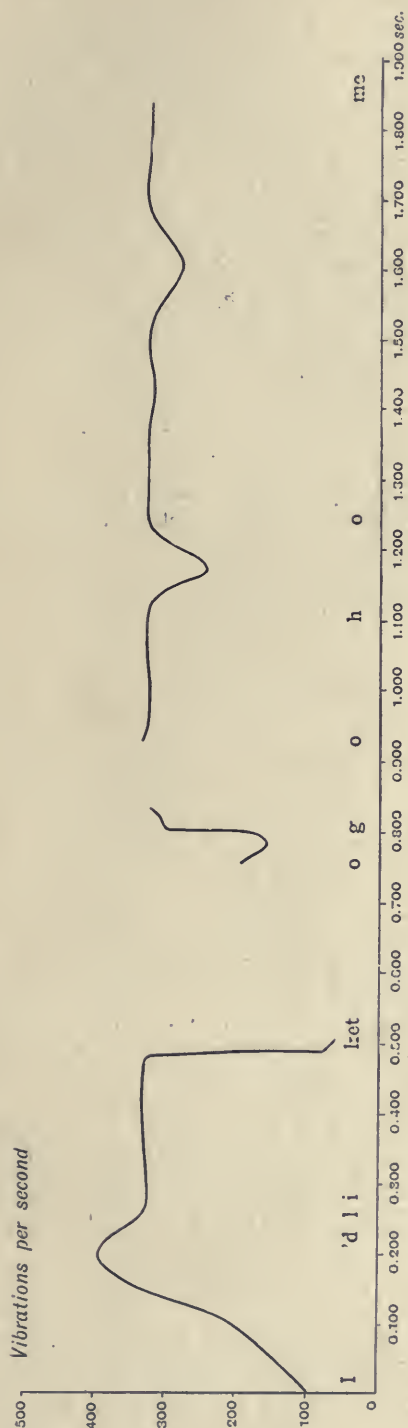


FIG. 18.—Melody plot to fig. 17. The tone rises rapidly from a low pitch of 100 to nearly 400. It finally settles on a pitch of about 325 which is the general pitch of the sentence. At the end of "I," it suddenly drops to a very deep pitch for two vibrations. When it starts again in "o" of "to" it again begins low and rises abruptly. There is some fluctuation in the remainder of the word, but in general the tone is quite monotonous, not even falling at the end.

long; there are peculiar laryngeal vibrations at the beginning, whereas normally there should be none whatever. The "t" shows a fairly good occlusion; it has a strong breathy explosion. The "ó" is longer than in the normal record. The "g" has a strong explosion, whereas in this sentence spoken normally it usually has a very faint one or none at all. The "o" thereafter is long. The "h" is sonant (as indicated by the small vibrations), as it often is normally between two vowels (see fig. 5). The second "o" is enormously lengthened; the rise and fall of the curve show slow variations of intensity. No vibrations could be distinguished in the "m"; it was either surd (i.e., with no laryngeal vibrations) or only faintly sonant.



FIG. 19.—Enlarged waves from fig. 17. Two long peculiar vibrations at the end of "i" in fig. 17 are shown greatly enlarged.

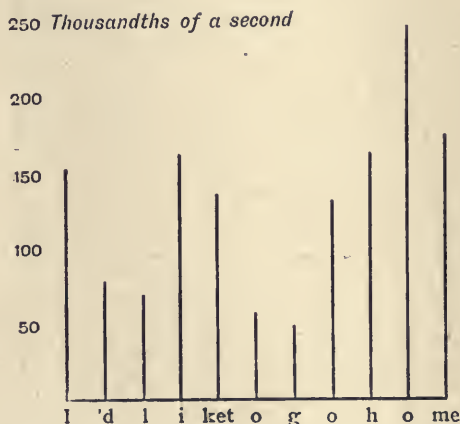


FIG. 20.—Duration Chart to fig. 5. The sounds "l," "i," "o," "h," "o," and "me" are longest; the others are short. The sounds of "k" and "t" cannot be separated.

The melody plot for fig. 17 is given in fig. 18. It shows that the voice starts very low at the beginning and rises rapidly by nearly two octaves. The general course of the melody is monotonous. The small fluctuations of normal melody are absent and the voice does not fall at the end.

The general monotony is presumably the result of spasticity of the laryngeal muscles. The low start and the rise over about two octaves in the initial vowel may be interpreted as due to the difficulty in getting the laryngeal muscles under proper control (ataxia plus anataxia).

At three places the melody plot shows marked interruptions by a fall of sometimes several octaves. Inspection of the original record at these points shows that the series of small regular vibrations is

650 Thousandths of a second

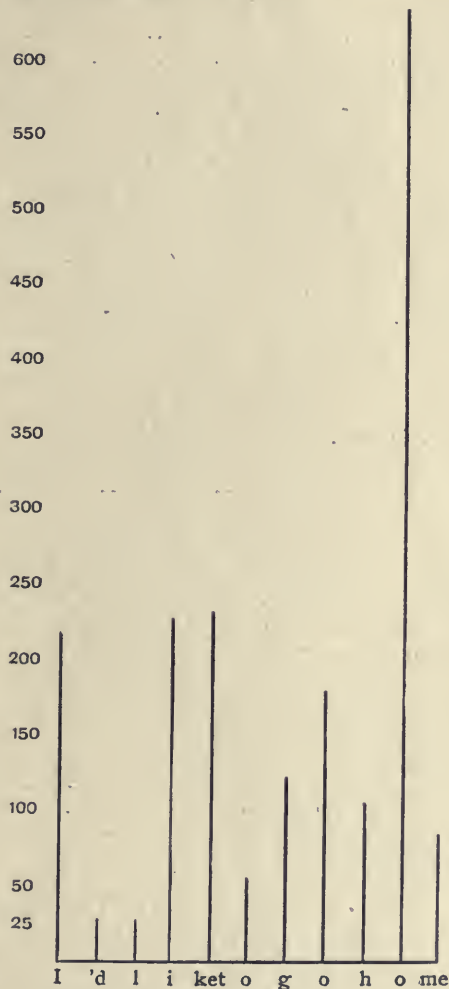


FIG. 21.—Duration Chart to fig. 17. Compared with fig. 20 the sounds of "I," "i," "kt," and the second "o" are slightly lengthened. The third "o" is enormously lengthened. Several of the sounds are shortened. The alteration of duration is quite irregular. It does not proceed on a system of proportionate lengthening as in ordinary slow speech. It does not exaggerate the differences between long and short sounds as in scanning. It does not bring each syllable out in equal times as in staccato speech. It does not separate the syllables or sounds by pauses.

suddenly interrupted by a few large irregular ones. One of these places is shown on an enlarged scale in fig. 19. These are the peculiar irregular vibrations discussed above.

The durations of the separate sounds are obtained by measuring their lengths in the records and turning the results into time by the time equation. The durations for the records in figs. 5 and 17 are as follows:—

	I	d	l	i	ket	o	g	o	h	o	me.
M. W. F. (normal)	.. 154	.. 77	.. 70	.. 161	.. 137	.. 59	.. 49	.. 132	.. 165	.. 247	.. 176
E. A. E. (dis. scl.)	.. 217	.. 27	.. 26	.. 227	.. 233	.. 51	.. 124	.. 180	.. 106	.. 633	.. 87

As explained above, the “e” of “like” and “home” represents no sound; the sounds of “k” and “t” are run together.

The results are expressed in the “duration charts” shown in figs. 20 and 21. Comparison of the charts shows: (1) that the sounds in the speech of E. A. E. are not all lengthened proportionately in the normal relations; (2) that they are not all of one length; (3) that the lengthening may affect vowels or consonants.

Separated into syllables in the usual way the durations would be as follows:—

	I'd	like	to	go	home.
M. W. F. (normal)	.. 231	.. 300	.. 127	.. 181	.. 588
E. A. E. (dis. scl.)	.. 244	.. 380	.. 177	.. 304	.. 739
Excess of E. A. E. over M. W. F.	.. 5 %	.. 27 %	.. 39 %	.. 70 %	.. 26 %

Patients with disseminated sclerosis frequently bring their syllables out in a laboured way that has been called “scanning.” Exactly similar speech is often found in hemiplegia, cerebral diplegia, &c.

The term “scanning” is applied in prosody to marking off the long and short or the loud and weak syllables, that is, to indicate the maxima and minima. In scanning a line of verse with the voice, the speaker exaggerates the differences between the two kinds of syllables, making the emphatic syllables more emphatic (longer or louder) and the unemphatic ones less marked (shorter or weaker). This is exactly what the patient with disseminated sclerosis does not do. She does not lengthen the long syllables and shorten the short ones; she does not give more intensity to the strong ones and less to the weak ones. Moreover she does not do exactly the opposite by making the unemphatic syllables more nearly equal to the emphatic ones, as has often been asserted. Finally, she does not bring each syllable out as a separate unit, as has been asserted by those who claim that the speech is “staccato.” She does not even produce the successive efforts at regular intervals. The speech is thus neither scanning nor anti-scanning, nor staccato nor rhythmic.

The records prove clearly that the successive efforts of emphasis show irregular variations in time that indicate a time-ataxia; there are

also greatly prolonged efforts that are exactly like those of spastic speech. We are justified in concluding that the speech, as far as the durations are concerned, simply shares in the general ataxia and spasticity and that its peculiarities are the results of ataxia and spasticity and the efforts to control them. The term "scanning speech" cannot be used.

§ 4.—NATURE OF SCLEROTIC SPEECH : DIAGNOSTIC TABLE ; EARLY DIAGNOSIS.

From the mass of accumulated records and measurements only typical examples have been reproduced. The conclusions drawn from them were verified for the others. The peculiar vibrations, the monotony, the defective rhythm, &c., were always present.

All these speech signs can be deduced from simple principles. The peculiar vibrations, the irregularities of breathing and the inaccuracy of enunciation are attributable to ataxia. The thickness of speech can be attributed to spasticity, or hypertonia, of the muscles of enunciation. Records and observations of spastic speech (infantile cerebral diplegia, hemiplegia, &c.) show that the condition of hypertonia and the effort to overcome it (anatonía) cause loss of ease of movement, monotony, slowness and alteration of enunciation. All the signs of sclerotic speech recorded up to the present can be explained as the results of ataxia, anataxia, hypertonia and anatonía.

Staccato speech has been found; it is shown to consist of ataxia plus anataxia of breath control. Scanning speech never occurs; when the rhythm of speech is disturbed, the alteration is in the direction of irregularity of rhythm. Pauses occur as the result of breath anataxia; the statement that the syllables are separated by pauses is simply not true. The statement of one authority that there is no characteristic defect for speech in this disease is quite excusable on account of the apparently disconnected and erratic forms in different patients; the records show, however, that they can all be reduced to the fundamental formula.

Owing to the great variations in the symptoms of disseminated sclerosis, it is frequently confused, particularly in its early stages, with other diseases.

The most common confusion is that with hysteria. Although the one consists of organic lesions of the central nervous system and the other is a purely psychical condition, and although the one usually runs an inevitable course where treatment is only palliative, and the

other can be modified or cured by proper mental or hygienic principles, yet at the present day there is frequently no possibility of making a decision as to which disease is present.

Elements	Disseminated sclerosis	Fatigue neurasthenia	General paralysis
I. Speed	Slow	Normal	Normal.
II. Loudness	Normal	Lessened	"
III. Fatigue	0 or +	+	0
IV. Rhythm :			
(a) Duration ..	Lessened	Normal	Normal.
(b) Stress	"	"	"
(c) Pitch	"	"	"
V. Breath	Irregular	"	Normal or finely irregular.
VI. Laryngeal tone :			
(a) Acoustic character	Clear	Normal or breathy, or tremulous	Normal.
(b) Pitch control ..	Irregular	Normal or tremulous	Normal or tremulous.
(c) Sentence melody	Monotonous	Normal or melancholy	Normal.
(d) Vowel melody ..	Lost in sentence monotony	Normal	"
VII. Enunciation :			
(a) Formation of sounds	Coarse irregularity	Normal or weak	Finely irregular.
(b) Co-ordination in duration	"	Normal	"
(c) Co-ordination in force	"	"	"
VIII. Combination of sounds:			
(a) Repetition ..	0	0	+
(b) Transposition ..	0	0	+
(c) Elision	0	0	+
(d) Insertion ..	0	0	+
IX. Ability to change :			
(a) Temporarily ..	0	+	0
(b) Permanently ..	0	+	0

(I) Speed is given by the length of a word or phrase as compared with the normal length.

(II) Loudness shows itself in larger curves in the records.

(III) Fatigue may show itself in a single word by decrease in loudness, or in a succession of records by cessation of speech, by tremulousness, &c.

(IV) Rhythm depends on relative duration of the syllables (long and short), relative stress (loud and weak) and relative pitch (high and low).

(V) Breathing affects the intensity and regularity of the sounds.

(VI) The laryngeal tone, or tone of the voice, has an acoustic character that is usually clear. Pitch control is shown by the ability to sing tones of different pitch. The sentence melody is the rise and fall of the voice in speaking a phrase or a sentence. The vowel melody is the rise or fall of tone within the individual vowels.

(VII) Enunciation: the formation of sounds requires certain very definite movements of lips, tongue, velum, &c., for each one. For a normal sound the muscular movements must have proper coordination in duration and proper coordination in force.

(VIII) Combination of sounds into words and phrases may be disturbed in the four ways indicated.

(IX) Ability to change. An abnormal mode of speech may be altered temporarily or permanently.

Disseminated sclerosis is also sometimes confused with encephalitis, cerebral-spinal lues, paralysis agitans, general paralysis, pseudo-sclérosis, &c. It is evident that a method would be of value which would definitely decide at the earliest moment whether the trouble is disseminated sclerosis or not. The presence of the peculiar vibrations in a speech record proves the existence of laryngeal ataxia and definitely excludes any of the diseases just mentioned. Laryngeal ataxia occurs in Friedreich's disease and possibly in others yet to be studied. The description of the speech in lenticular degeneration does not seem to indicate anything like that in disseminated sclerosis. I have seen one case that had been diagnosed as lenticular disease; the speech was plainly sclerotic and the diagnosis was a mistake.

The annexed table gives the speech characteristics that are present in disseminated sclerosis when the speech is affected to a noticeable degree. The analyses of two other diseases are added for comparison.

In conclusion it is my most agreeable duty to acknowledge obligations to Dr. F. E. Batten for the use of a consulting room at the National Hospital, for access to many cases with speech defects and for helpful suggestions; to Dr. F. W. Mott and Dr. R. Armstrong-Jones for the Claybury case; and to the National Medical Research Committee for some aid in defraying expenses.

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THE FACTORS WHICH GOVERN THE PENETRATION OF
ARSENIC (SALVARSAN) AND ANILINE DYES INTO
THE BRAIN AND THEIR BEARING UPON THE
TREATMENT OF CEREBRAL SYPHILIS.¹

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In a previous paper [2] we have shown that after intravenous injections of salvarsan and neosalvarsan no arsenic can be found in the brain substance, this result being due not to any lack of affinity between the brain-cells and the drug, but to an obstruction to the passage of the drug from the blood-stream into the brain substance.

In the present paper we detail experiments which we have devised to throw light upon the factors involved in penetration or lack of penetration into the brain. We required for this investigation a group of substances which were relatively non-toxic when injected intravenously and readily recognizable in the tissues after the death of the animal. Various dyes, some of which had already been investigated by Ehrlich, were selected for our purpose.

Our mode of procedure was as follows :—

A rabbit was injected intravenously with a large dose of an aniline dye and killed about five minutes later by air embolism—10 c.c. of air being injected into the ear vein. The animal was then dissected and the distribution of the stain noted in the tissues generally. The brain and cord were next exposed and examined. The cerebrospinal fluid was collected in a capillary pipette by puncture of the membranes after exposure of the cord; by this method the fluid may be obtained

¹ Work carried out under grants from the Medical Research Committee.

macroscopically free from blood. The pipettes were viewed along their long axis in order that small traces of stains might be detected.

By the method of intravenous injection stains may be divided into two groups, namely, those which stain the central nervous system and those which do not.

Group I.—STAINS WHICH COLOUR THE TISSUES GENERALLY AND ALSO THE CENTRAL NERVOUS SYSTEM.

(1) *Methylene Blue.*

This stain was used as an intravital stain by Ehrlich. It is very rapidly reduced to a colourless compound by the tissues, and this fact must be borne in mind when investigating its distribution within the body.

The effect of methylene blue is as follows:—

Experiment 1.—A rabbit (1,300 gm.) was injected intravenously with 1.5 c.c. of a saturated solution of methylene blue (“medicinal pure” Grübler). The animal immediately became restless and tinged with blue. This coloration rapidly passed off and the symptoms were disappearing when the rabbit was killed by air embolism five minutes after the injection. The internal organs were examined immediately and found to be uncoloured, but the muscles were slightly blue and this became intensified on exposure to air.

The membranes of the brain and cord were uncoloured, the cerebro-spinal fluid was also uncoloured and remained so even after the addition of hydrogen peroxide. The brain was at first colourless, but on exposure to air became distinctly blue; the cord on the other hand was uncoloured and remained so.

The brain and cord were placed in Bethe’s solution² for the fixation of methylene blue. The blue colour then became more intense and was seen to be confined to the grey matter of both structures. After fixation and embedding in paraffin sections were cut and the blue staining was found to be diffuse. No intracellular granules were observed and no differential staining of the tissues.

Experiment 2.—In a second experiment a rabbit (2,000 gm.) was injected with a larger dose, 10 c.c., of a saturated solution. Toxic symptoms were more profound, but were passing off when the animal was killed five minutes later.

² Dissolve ammonium molybdate (1 gm.) in 10 c.c. of distilled water and add 1 c.c. of hydrogen peroxide—the solution will become yellow—then add one drop of hydrochloric acid.

The appearance of the tissues was similar, although in this case the lungs were distinctly stained.

Thus, after the injection of methylene blue the distribution of the stain in the central nervous system is as follows: Meninges, unstained; cerebrospinal fluid, unstained; grey matter, stained diffusely, no granules; white matter, unstained.

(2) *Neutral Red.*

This stain was also used by Ehrlich for intravital purposes. It has very little toxicity, and is rapidly excreted by the kidneys.

Experiment 3.—A rabbit (1,500 grm.) was injected intravenously with 15 c.c. of a saturated solution of neutral red (Grübler, "for intravital injection"); tetanic spasms came on before the injection was finished and rapidly increased until complete rigidity was present. These symptoms, however, soon began to pass off and the animal was killed ten minutes later. General staining was present externally.

On dissection the organs were found to be stained, the liver and kidneys being dark purple and the muscles bright red.

The meninges of the central nervous system were slightly pink, but the cerebrospinal fluid was entirely colourless. The brain, on the other hand, was intensely stained a dark red, while the cord was pink. Incisions into the brain and cord showed that the colour was confined to the grey matter. Portions were fixed in formalin and embedded in paraffin. In sections the coloration of the grey matter was found to be diffuse, although there appeared to be a slight differential staining of the cortical layer of the ganglion cells. No granules, however, were observed in these cells.

Experiment 4.—In a further experiment a rabbit (1,600 grm.) was injected with 7 c.c. of the saturated solution and an exactly similar distribution of the stain was found. In this case, however, a slight coloration was present in the cerebrospinal fluid due to a small admixture of blood.

Amongst the other stains which affected the grey matter of the central nervous system were alizarin blue and malachite green; while indophenol and aurantia did so only slightly. In no case, however, was the effect quite so marked as with neutral red and methylene blue, perhaps because the less solubility and greater toxicity did not allow of their use in such large doses.

Group II.—STAINS WHICH COLOUR THE TISSUES GENERALLY, BUT NOT THE CENTRAL NERVOUS SYSTEM.

(1) *Fluorescine.*

Experiment 5.—A rabbit (1,500 gm.) was injected intravenously with 5 c.c. of an alkaline watery solution of fluorescine (1 per cent.). No toxic symptoms followed and the animal, distinctly yellow, was killed after five minutes by air embolism.

On examination the internal organs were slightly yellow, while the kidneys were intensely stained. The muscles were golden yellow.

On exposing the central nervous system, the meninges were found to be stained but the cerebrospinal fluid was quite colourless. Both the brain and the spinal cord were entirely free from colour.

Experiment 6.—Another rabbit (1,500 gm.) was injected with 10 c.c. of the same solution of fluorescine. Exactly similar results were obtained as in the last experiment, that is, the brain and cord were unstained while the meninges were stained. In the cerebrospinal fluid a trace of fluorescine was detected, due, no doubt, to the presence of a slight quantity of blood which could be detected by the microscope.

(2) *Indigo-carmin.*

Experiment 7.—A rabbit (1,800 gm.) was injected with 20 c.c. of a saturated solution of indigo-carmin in saline solution. No toxic symptoms appeared and the animal became tinged green. In five minutes it was killed.

The internal organs and muscles were stained green. The meninges of the brain and cord were distinctly coloured, but the cerebrospinal fluid and the nerve tissue were entirely unstained.

Other stains which did not colour the central nervous system were found to be acid fuchsin, light green, trypan red, trypan blue, and pyrrhol blue.

From our experiments, a number of which have been given above, it is clear that the aniline dyes tested may be classified according as to whether, on intravenous injection, they stain the nervous tissues or not, and an examination of the physical properties of these substances might reveal the factors by virtue of which one group stains while the other does not.

From analogy with our experiments with salvarsan we argued that one stain did not colour the brain, while another did, because the former

did not penetrate. The blood capillaries of the brain are peculiar when compared with those of other parts of the body, in that they are surrounded by an extra adventitial sheath, and we supposed that this extra sheath might act as a barrier to certain drugs while permitting the passage of others. We therefore investigated the chemical formulæ of these stains, but were unable to find any atomic arrangement which was characteristic of the two groups.

Similarly the diffusibility of the stains did not correspond with their staining reactions.

The question of solubility appeared to be of more importance. Ehrlich [1] stated that neurotropic substances are lipotropic, and Overton [3] that before a substance could penetrate into a cell it must be soluble in the cell membrane, and these membranes being lipoids it follows that such a substance must be soluble in lipoid solvents such as alcohol and ether. The solubility of the dyes which we used in alcohol and ether did not correspond with their staining reactions, but when we used chloroform as a solvent we found that those stains which coloured the brain were soluble in chloroform, while those which did not were insoluble. It would appear, therefore, that the solubility in chloroform or related substances is an important factor in determining a passage from the blood into the nervous tissues or not.

On applying this test to salvarsan we found that neither salvarsan nor neosalvarsan were soluble in chloroform; we are, therefore, inclined to believe that this fact can account for their absence from the brain.

In order to test this suggestion we have examined a large number of organic and inorganic arsenical compounds, for the majority of which we have to thank Miss F. M. G. Micklethwait, Imperial College of Science. No very striking result was obtained, due no doubt to the fact that hardly any of these compounds were soluble in chloroform, and the few which were, were either completely insoluble in water or immediately hydrolysed by it. Certain combinations, however, of arsenic and aniline colour bases gave encouraging results, and after their administration arsenic was demonstrable in the brain, but owing to the War the work had necessarily to be suspended in this interesting stage.

CONCLUSIONS.

(1) Certain dye substances can pass directly from the blood to the brain substance proper without being found in the cerebrospinal fluid, while others fail to penetrate into the brain.

(2) The chief factor which governs the passage of the dyes is their solubility reactions.

(3) This is a peculiar solubility and not a general lipoid solubility.

(4) It corresponds to a solubility in chloroform and in water or perhaps to their partition coefficient in these liquids.

(5) The present-day arsenical remedies are, to some extent, inefficient in the treatment of syphilis of the central nervous system because they do not possess the necessary solubility to allow them to pass from the blood-vessels into the brain substance. Their relative inefficiency has nothing to do with their absence from the cerebrospinal fluid.

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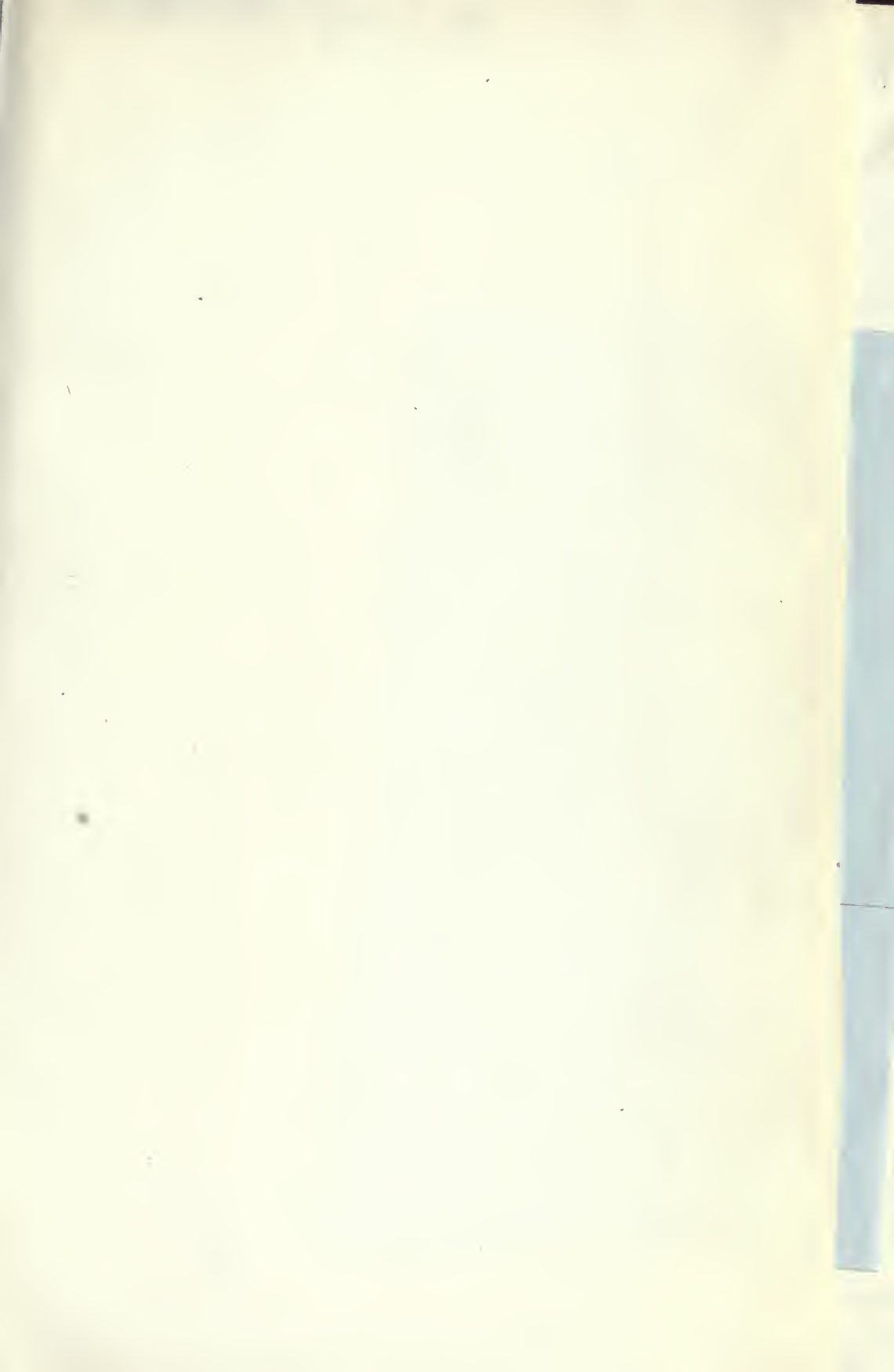
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